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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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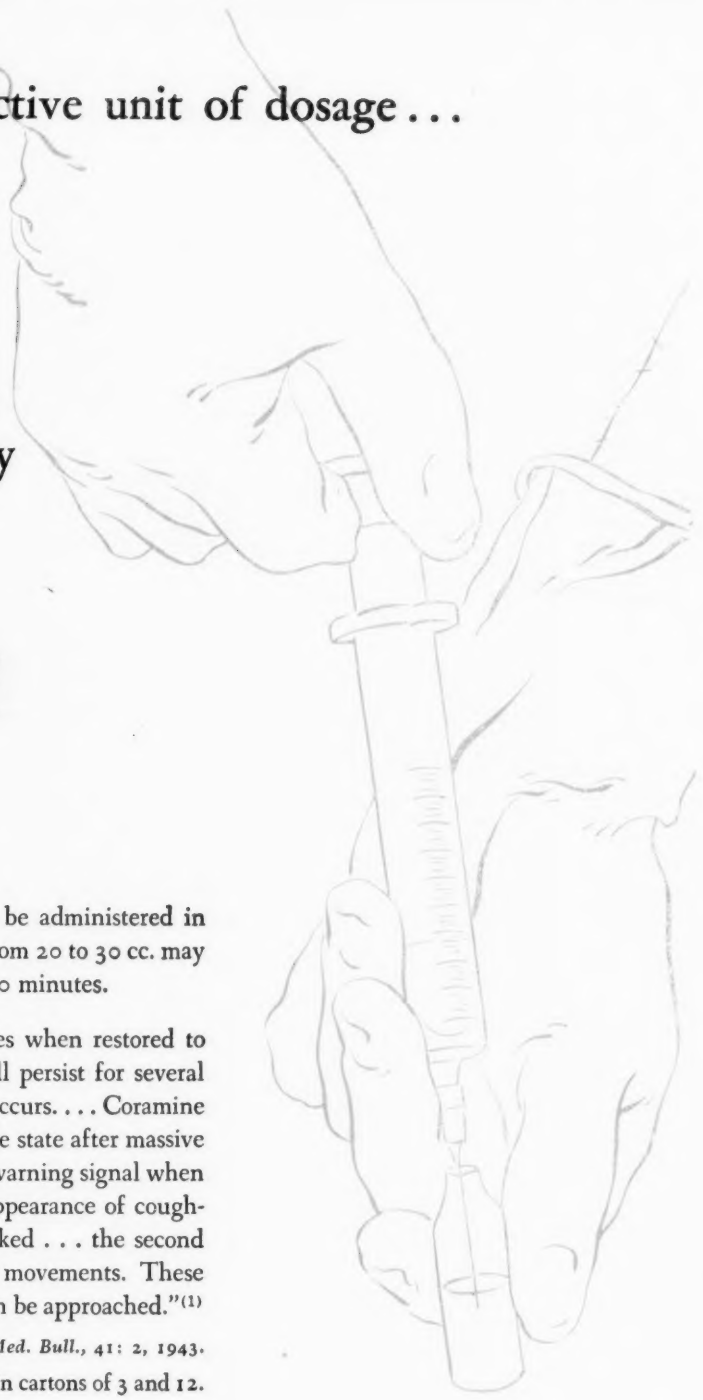

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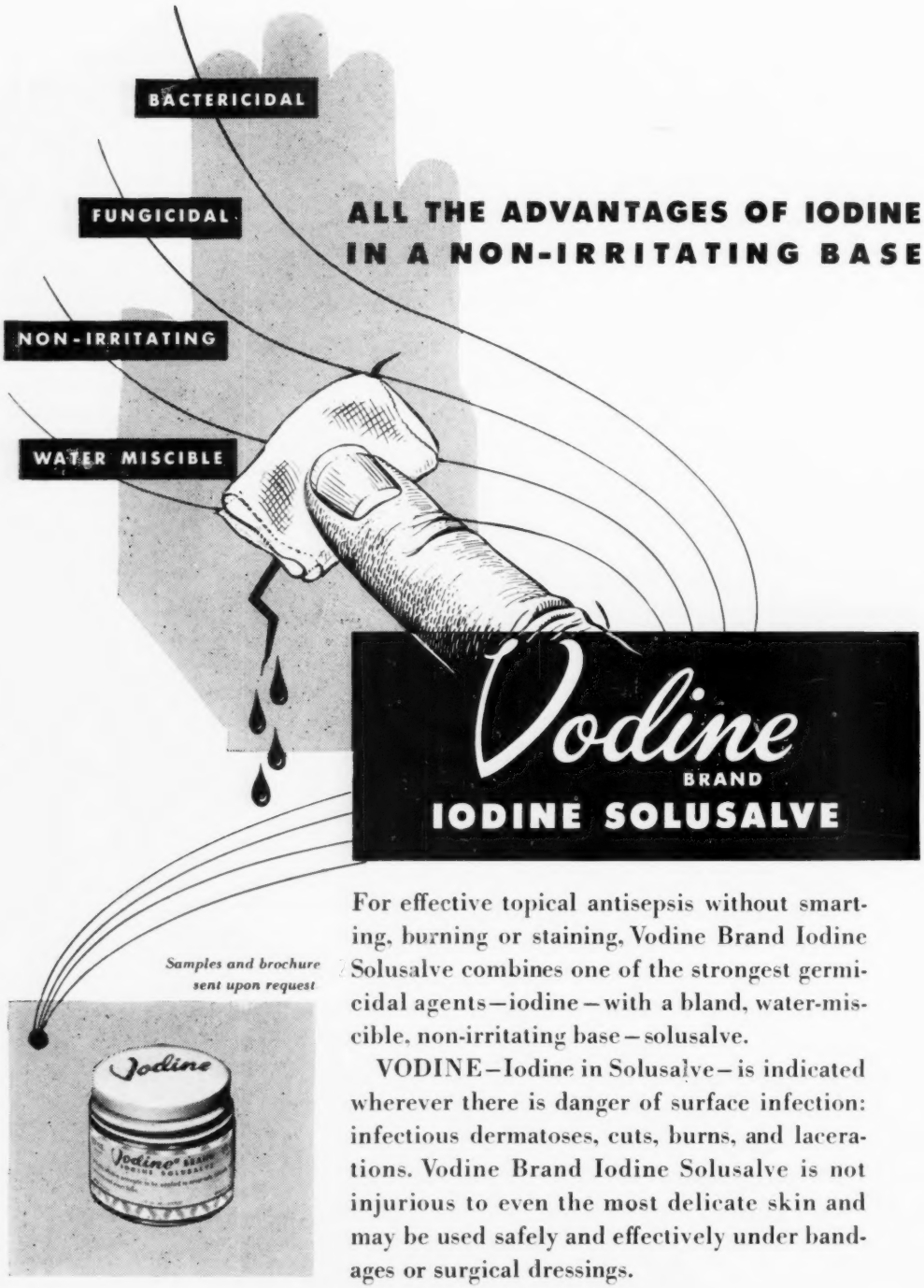

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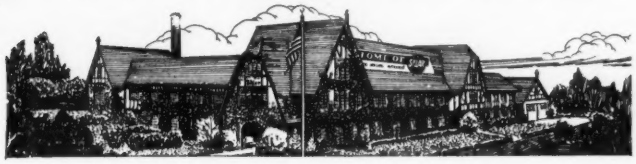

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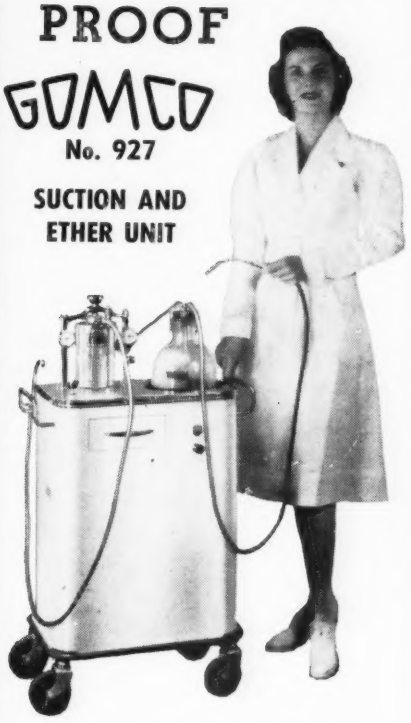

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Original Communications

RESECTION OF THORACIC ESOPHAGUS FOR CARCINOMA LOCATED ABOVE ARCH OF AORTA: CERVICAL ESOPHAGOGASTROSTOMY

JOHN H. GARLOCK, M.D., NEW YORK, N. Y.

(From the Surgical Service, Mount Sinai Hospital)

IT IS fortunate that the least frequent site for cancer to attack the esophagus is that portion of the organ located between the superior border of the aortic arch and the apex of the chest or root of the neck, an area termed the superior mediastinum. It has been known for many years that this portion of the esophagus is difficult to approach surgically. It will be remembered that, at this location, the esophagus lies posterior and to the left of the trachea, and mesial to the left great vessels, and is in close proximity to both vagus and recurrent laryngeal nerves. The thoracic duct begins to swing outward to the left and is not in as close contact with the esophagus as it is behind the arch of the aorta. Many years ago Zaaijer, Küttner, and Sauerbruch attempted to excise carcinomas of the esophagus in this location by utilizing an anterior approach, splitting the clavicle and upper ribs. Although the exposure was adequate, it was unnecessarily mutilating and the operation was never completed from the standpoint of re-establishing gastrointestinal continuity.

Unfortunately, tumors in this location are all too frequently locally inoperable when the patients first consult the surgeon. A tumor growing in a peripheral direction will soon involve the left recurrent laryngeal nerve, vagus nerve, or trachea. There may be extensive involvement of the cervical lymph nodes. It has been our experience that local inoperability is found more frequently with tumors in this location than with any other portion of the organ. Therefore, the opportunity to carry out a radical resection will be infrequent. Still, the surgeon should have at his command an operative procedure which can be utilized for the infrequently operable case and which embodies all the recently developed concepts of the rational surgical treatment of malignancy of other portions of the esophagus. It is for this reason that I would like to describe an operative procedure that was utilized to excise a large intraluminal fungating tumor in this location with re-establishment of esophagogastric continuity by uniting the transplanted stomach to the remains of the esophagus in the neck.

Received for publication, Nov. 17, 1947.

It seems unnecessary to stress the fact that the surgeon should use every expedient to determine operability before subjecting the patient to exploration. Preoperative studies should include careful chest roentgenograms, laryngeal examination to disclose left recurrent nerve involvement, bronchoscopy to indicate tracheal infiltration, and circulatory studies to exclude vagus nerve invasion. Palpatory examination of the neck will indicate the presence or absence of metastatic nodes. If any of the mentioned structures are found to be definitely invaded by the growth, exploration should not be undertaken.

From the standpoint of disturbed physiology, any operative manipulation on the esophagus in this location, especially if the tumor is a large one and extends toward the right side of the mediastinum, has one dangerous feature which the surgeon must appreciate thoroughly. I refer to the inadvertent stimulation of both vagus nerves in their supracardiac location, something which the surgeon may find impossible to avoid if he is to remove completely the tumor-bearing part of the esophagus. Such stimulation may set up the so-called vagovagal reflex which may result in irreversible disturbances of cardiac function and cause death of the patient. This is what I believe happened to the patient reported in this paper. Whether thorough preoperative and operative atropinization will prevent this serious complication remains to be seen. My physiologist friends tell me that atropine should be good insurance against this eventuality. Further experience is needed to settle this point.

CASE REPORT

Mrs. D. B. (Hospital No. 558268), aged 46 years, was admitted to Mount Sinai Hospital on Dec. 24, 1946, complaining of dysphagia of three months' duration. The dysphagia originally was noted when swallowing solid food and was accompanied by substernal pain indicated at the upper sternal region. At the time of admission, the patient was able to swallow only liquids. There had been a loss of fifteen pounds. The past and personal histories were negative. Her mother had died of carcinoma of the uterus.

Physical Examination.—Examination indicated a rather obese woman not appearing ill. There was nothing abnormal to be felt in the neck. Heart findings were negative, pulse was 88, abdomen and pelvis findings were negative. Blood pressure was systolic 130 mm.; diastolic 90 mm.

Laboratory Work-up.—Laboratory studies showed hemoglobin 100 per cent; white blood cells 12,080 with a normal differential. Electrocardiogram was negative. X-ray examination of the chest showed negative results. Roentgenographic examination of the esophagus showed a large irregular mass which partially obstructed the esophagus at the upper level of the aortic arch.

Esophagoscopy.—At 18 cm. from the upper incisor teeth was found a large irregular grayish tumor which, on biopsy, proved to be an infiltrating hornifying squamous cell carcinoma.

Vital Capacity.—Vital capacity was found to be 2.4 liters, or 74 per cent.

Preoperative.—Preoperative preparation consisted of a high caloric fluid intake, parenteral vitamins, aerosol penicillin nebulization of trachea and bronchi for six days, and mechanical washing of the esophagus through a Levin tube.

Operation.—Operation was done Jan. 3, 1947, under intratracheal gas-oxygen-ether anesthesia. The patient was placed on the operating table in such a way as to incline the left side upward and somewhat toward the table, exposing simultaneously the upper abdomen,

thorax, and neck. This entire area was prepared and draped for simultaneous accessibility to chest and neck. An oblique incision was made along the left sternomastoid muscle. By retracting the left lobe of the thyroid, access was gained to the posterior mediastinum. By blunt finger dissection, the superior mediastinum was palpated. The upper half of the tumor could be delineated with ease and it was decided that the tumor was resectable. The cervical wound was then closed temporarily.

Thoracic Stage.—A long incision was made over the left seventh rib which was resected subperiosteally (Fig. 1). A widely opened rib spreader gave excellent exposure of the entire left side of the chest. The mediastinal pleura was then incised above and below the aortic arch. There was disclosed a large tumor of the esophagus starting about the level of the middle of the arch and extending upward to a point about one inch above the arch. The tumor projected more into the lumen than toward the periphery of the organ and extended

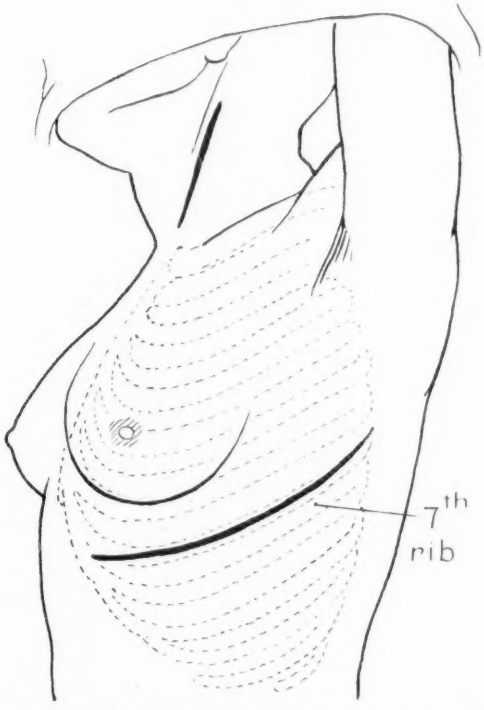

Fig. 1.—Diagrammatic sketch showing thoracic incision over the seventh rib which is removed subperiosteally.

to the right side of the mediastinum. It measured about two inches in its transverse diameter. After a great deal of difficulty it was dissected free from surrounding structures. During this process, the left vagus and recurrent nerves and the thoracic duct were visualized and protected. The right nerves were never seen. The phrenic nerve was pinched to immobilize the left leaf of the diaphragm. The latter structure was then incised radially from the esophageal hiatus outward. The cardiac end of the stomach was freed from the diaphragm and the whole stomach was mobilized by ligating and dividing the vasa brevia, the left gastroepiploic vessels, and left gastric artery at its origin from the celiac axis. The gastrocolic ligament was left attached to the stomach to preserve the entire gastroepiploic arch. The stomach was thus freed as far as the pylorus. No enlarged lymph nodes were found.

The esophagus was divided at the cardiac junction and the opening in the stomach closed with two layers of silk sutures (Fig. 2). The mobilized esophagus was brought up from behind the arch of the aorta so as to lie in a completely supra-aortic position. The neck wound was then reopened and the mobilized thoracic esophagus was brought out of the neck wound, care being taken not to compromise the esophageal branches of the inferior thyroid artery. The neck area was covered temporarily and the thoracic part of the operation was then completed. The mobilized stomach was brought to the apex of the chest. It was found that the upper three inches of the organ could be pushed through the apex of the chest into the neck without any tension whatsoever and without demonstrable interference of blood supply. Two

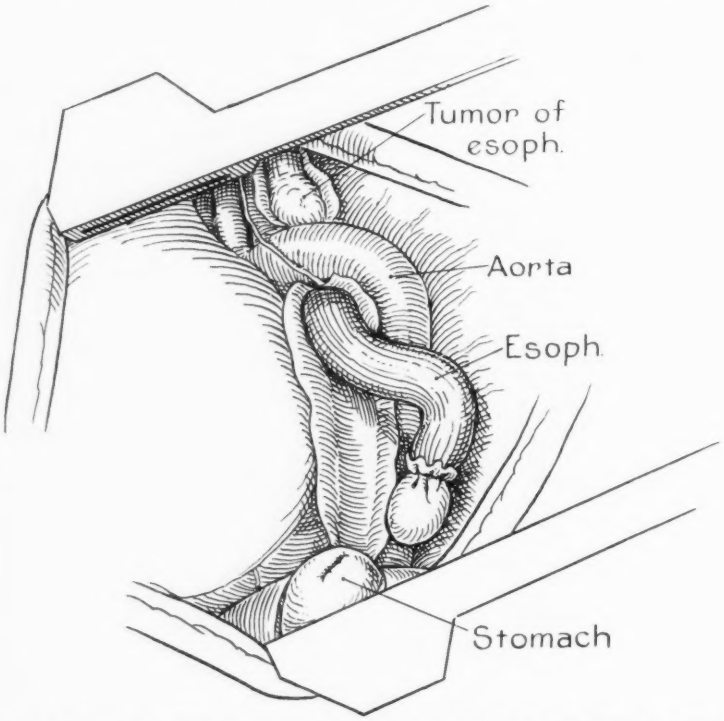

Fig. 2.—The esophagus has been mobilized and radial incision made in the left leaf of the diaphragm. Transection was done at cardioesophageal junction with double inversion of the cardia and mobilization of tumor-bearing portion of esophagus above arch of aorta.

guide sutures of silk were then placed in the end of the stomach to be utilized for the anastomosis and these were withdrawn from the neck wound, thus helping to apply the proper amount of tension on the transplanted stomach (Fig. 3). The latter was anchored in its new position by a series of silk sutures between stomach and both edges of the mediastinal pleura (Fig. 4). The diaphragm was repaired around the transplanted stomach. A rubber tube was placed in the ninth interspace for underwater drainage and the chest wound was closed in layers.

Cervical Stage.—The patient was turned on the back and the neck wound was reopened. The esophagus was divided well above the tumor and the cardial portion of the stomach identified by the guide sutures was approximated to the esophageal stump with ease (Fig. 5). The usual two-layer interrupted silk suture anastomosis was then effected (Fig. 6). The stomach was anchored to neighboring areolar tissue in the base of the neck to prevent any drag on the anastomosis. Gauze packing was inserted to obliterate the opening in the apical pleura and the neck was closed around it (Fig. 7).

During the course of the operation, which lasted four and one-half hours, the patient was given 1,500 c.c. of whole blood. At the outset the blood pressure was systolic 120 and

diastolic 70, with a pulse of 110. At the end of the operation the systolic pressure was 80 and the diastolic 40. The pulse was 110. The graph of the blood pressure and pulse maintained a remarkably even line. At 9:45 P.M., pulse was 100; at 10 P.M., pulse 80, blood pressure 120/70; at 10:45 P.M., pulse 102, condition excellent; at 11 P.M., pulse 96, blood pressure 102/64; at 12 midnight, pulse 106; at 6 A.M., pulse 100. At no time was there any evidence of shock. Later in the morning the patient developed marked cyanosis accompanied by respiratory distress and died very quickly.

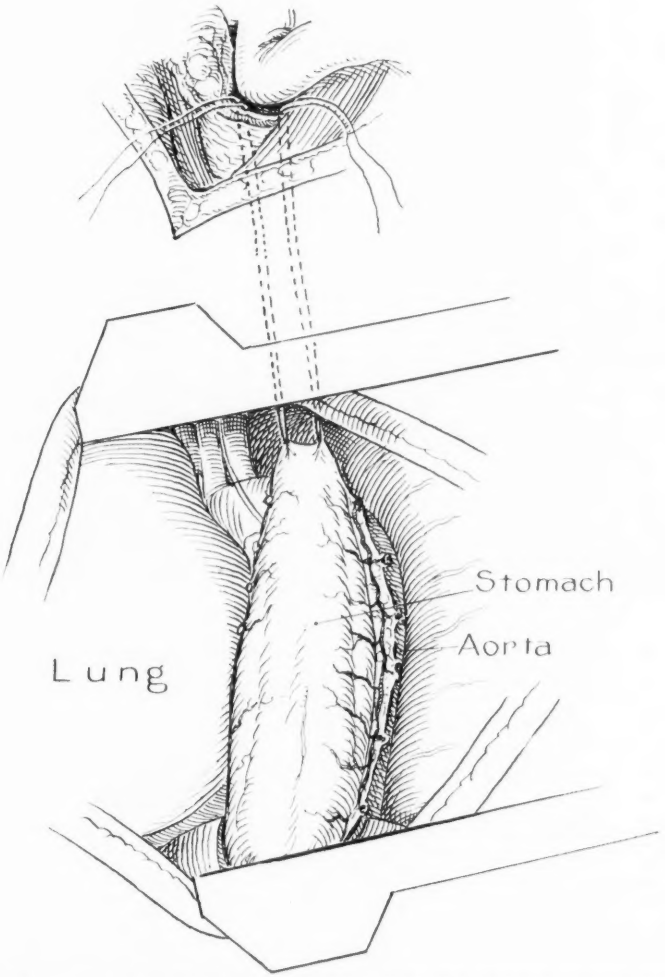

Fig. 3.—The stomach has been mobilized as far as the pylorus leaving intact the gastro-epiploic arch. Two guide sutures placed in the cardiac region are being pulled through the neck incision.

A complete post-mortem examination did not reveal any cause of death. The anastomosis was intact and the blood supply of the stomach in its new position was excellent. It is believed that the patient's death was caused by profound physiologic disturbances, possibly caused by vagal stimulation.

COMMENT

The operation reported in this paper seems a natural sequence of the operation I described two years ago for carcinoma of the middle third of the esophagus with esophagogastric anastomosis above the arch of the aorta. I do not

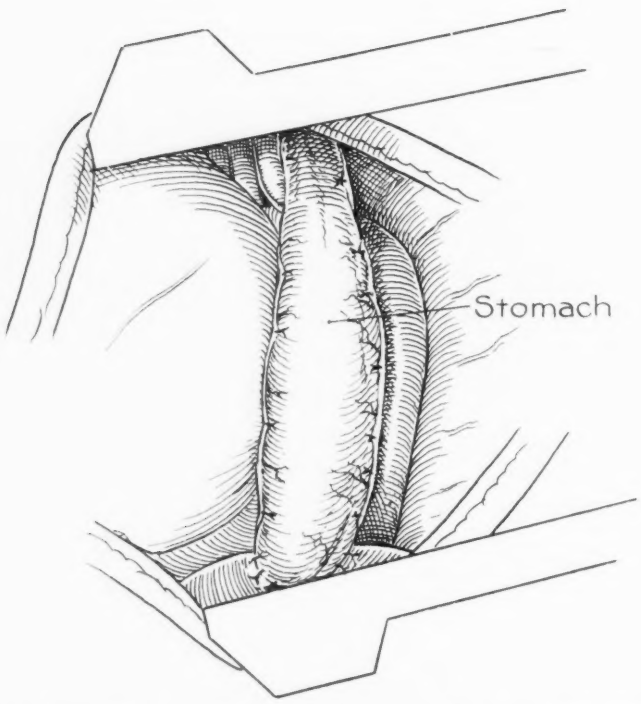

Fig. 4.—After sufficient stomach has been withdrawn through the lower angle of the neck incision, the stomach is now fixed to the cut edges of the mediastinal pleura and the opening in the diaphragm is being repaired around the transplanted stomach.

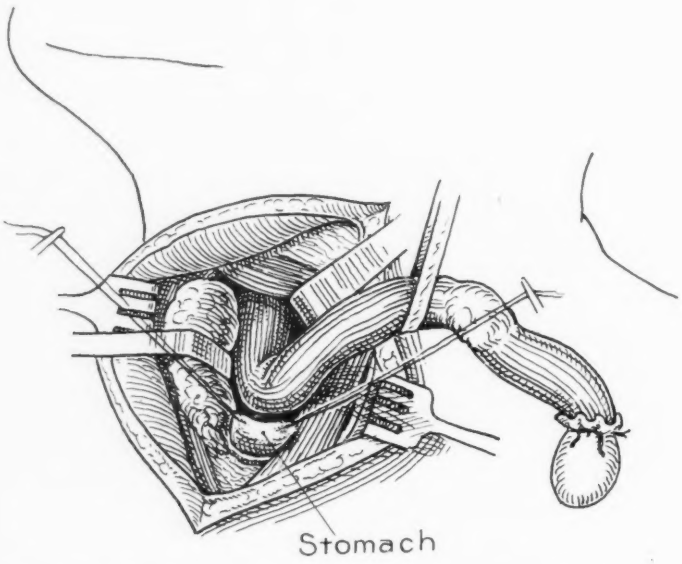

Fig. 5.—This diagram indicates the upper end of the stomach in the lower angle of the incision being approximated to the esophagus.

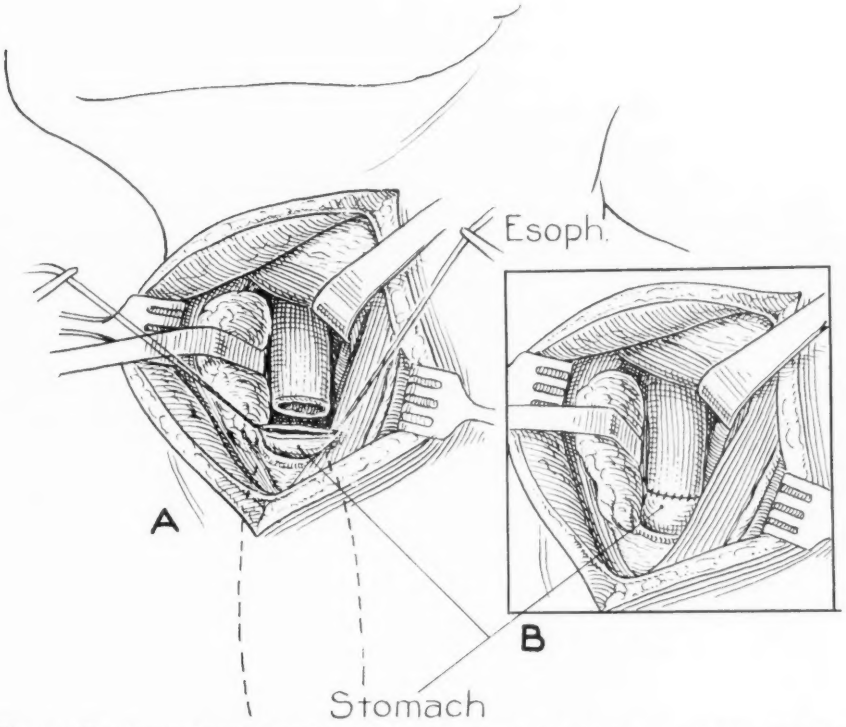

Fig. 6.—The tumor-bearing portion of the esophagus has been removed and an end-to-side anastomosis affected between the stump of the esophagus and the stomach, using two layers of interrupted silk sutures.

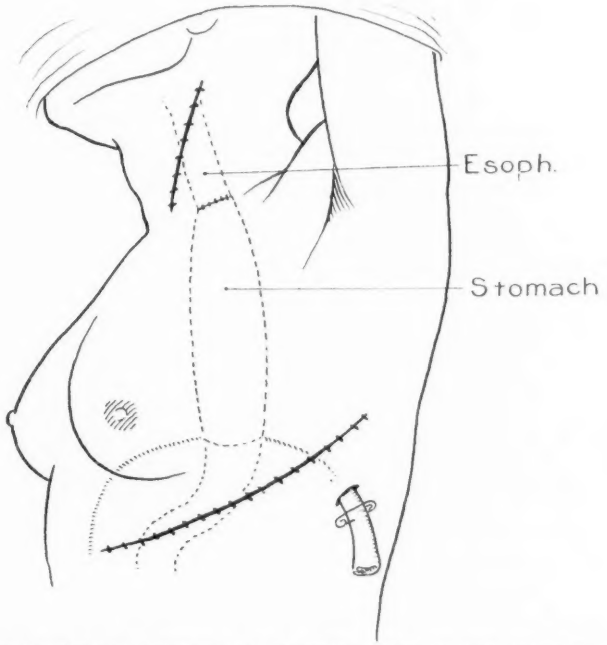

Fig. 7.—Diagrammatic sketch showing the transplantation of the stomach through the chest into the lower cervical region with anastomosis of the stomach to the esophagus.

believe that there is any increased danger to the blood supply of the stomach by bringing part of the organ into the neck through the superior aperture of the thorax. This case demonstrates that, in the patient of average height, the stomach can be mobilized sufficiently to permit its tranplantation above the apex of the chest without impairment of its vitality. The blood supply of the stump of the esophagus in the neck can be assured by preservation of the esophageal branches of the inferior thyroid artery. If on further trial this operation proves to be feasible, it will be unnecessary to employ the multiple procedures needed for transplantation of a loop of jejunum to bridge the defect between stomach and neck. This operation originally described by Lexer years ago, has been recently revived by the Russian surgeon, Yudin, Longmire and others. These procedures are fraught with considerable danger, first, from the standpoint of vitality of the transplanted jejunum, second from the standpoint of healing between stomach and jejunum and esophagus and jejunum with the ever present risk of fistula formation, and finally because of the real danger of stricture at the two sites of anastomosis. To overcome the first difficulty, Longmire recently advocated a direct anastomosis between the internal mammary artery and thel mesenteric vessels of the loop of jejunum. The use of the stomach as herewith reported would make all of these maneuvers completely unnecessary. It is probable that this operation could be utilized also for extensive impermeable lye strictures of the thoracic esophagus in the same way as Sweet employed the supra-aortic anastomosis for a lye stricture in the middle third of the organ. If this operation proves to be feasible, all of our problems concerned with malignancy of various segments of the esophagus will be greatly simplified. Only by a process of trial and error can we arrive at a common denominator in the successful surgical therapy of this disease.

COMBINED LEFT ABDOMINAL AND RIGHT THORACIC APPROACH TO RESECTION OF ESOPHAGEAL NEOPLASMS

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DURING the four years from 1944 to 1947 increasing success has been experienced in the resection of neoplastic lesions of the esophagus with re-establishment of the continuity of the intestinal tract. Many factors have been responsible for this: (1) The development and administration of anesthetics by highly trained medical personnel acutely aware of the physiological abnormalities created by the open thorax; (2) the better understanding by those preparing these patients for surgery of the importance not only of nutritional factors such as protein and vitamin replacement, but also of restoring depleted blood volumes, by transfusions before the patient arrives at surgery; (3) the proper use of the antibiotics; (4) the use of large volumes of blood during surgery; (5) the increased knowledge of thoracic surgery and the appreciation of those practices in operative technique and postoperative care which prevent, or at least minimize, many of the complications of this type of surgery.

Many operative approaches have been used in the resection of lesions of the middle and lower esophagus with the purpose of performing as complete a cancer operation as was feasible and yet, by re-establishing the continuity of the intestinal tract, provide for at least palliation should a cure not be possible. The left transthoracic approach and the thoraco-abdominal incisions used by Sweet[1] and Garlock[2] for the lower esophagus have perhaps been the best outlined in the recent literature.

There are a few very outstanding disadvantages, however, to the conventional approaches through the left thorax whether they be purely transthoracic or include an extension through the costal arch into and through the abdominal parietes. If the transthoracic approach has been used without a preliminary abdominal exploration, the operator may subject the patient to a major procedure only to find after the thorax and the diaphragm have been opened that the lesion has already involved the liver. Again when resecting lesions in the lower third of the esophagus one frequently has a tendency to divide the esophagus on the cephalad side much too close to the neoplastic process because for each higher level of transection the subsequent anastomosis becomes increasingly difficult to perform technically and one reaches a level about the seventh dorsal vertebra where the esophagus had better be passed behind the arch of the aorta and carried anteriorly to it to complete the anastomosis. This additional amount of surgery does increase the mortality of the procedure perhaps at least partially because of disturbed pulmonary and cardiac reflexes resulting from unavoidable trauma

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to the mediastinal nerve plexuses and from reflexes arising from the aortic arch which must be partially mobilized to effect the transfer of the esophagus anteriorly. In our earlier cases, perhaps for this reason, transection was, on occasion, too close to the gross lesion. Sections taken through the transected margin of some of these have shown neoplastic cells in the submucosa. This of course has been noted by many others.

A third factor which becomes of some importance in middle third lesions bear comment. It is not uncommon to find the lesion adherent to the right mediastinal pleural reflection. At the lower border of the fourth dorsal vertebra, the azygos vein arches forward across the esophagus to drain into the superior vena cava. Lesions which are adherent to this larger vein when approached through the left side of the chest beneath the lung root are technically very difficult and hazardous to remove without the constant danger of serious bleeding even when the opposite (right) side of the thorax is deliberately opened to facilitate this dissection. When operating through the left side of the chest the diaphragm of course must be opened widely. In so doing, if one does not crush the phrenic nerve one cuts across most of its branches near the hiatus which serves to make it functionless for many months and in some cases permanently. The quiet diaphragm is helpful during the operative procedure, but postoperatively this state is believed to be a disadvantage. Its abnormal position makes it difficult to detect supra- and infradiaphragmatic collections of fluid in the costophrenic angles on this side. It favors the development of atelectasis in the lower lobe with perhaps, at times, permanent crippling of this lobe through formation of adhesions between the collapsed lobe and the intrathoracic stomach. (The early stages of this pathology have been seen in one case at autopsy.) Perhaps the most serious physiologic effect is the loss of tussive power. In a small series of fourteen completed resections done through the left side of the thorax the incidence of patchy areas of pneumonitis has been large (over 50 per cent). The problem of urging and stimulating these patients to cough effectively postoperatively has been a real one and some of this difficulty doubtless is due to the loss of tussive power attending complete paralysis of the left half of the diaphragm.

In an effort to avoid many of these difficulties two cadaver dissections were undertaken with the purpose of exploring the advantages and feasibility of a combined approach, using a left upper abdominal and a right transthoracic approach through the bed of the seventh rib. In the dissections it was found necessary to divide the right crus of the diaphragm posterior to the position of the right phrenic nerve on the diaphragm. Otherwise the technique used was identical to one published by Ivor Lewis[3] in 1946. This combined approach was carried out on two patients and it was surprising to observe that the operation seemed technically less tedious, maintained its status as a cancer operation, preserved the phrenic nerve function bilaterally, did not require radical incisions in the diaphragm, allowed one to transect

the esophagus at any desired level and effect an anastomosis without interference with the aortic arch, resulted in less total gross trauma to the patient's tissues, and consumed less operating time. Postoperatively, the tussive power was well preserved in both patients.

One cannot develop a thesis on two cases and such is definitely not intended. Nor is this approach presented as an original contribution, for Ivor Lewis,[3] the British surgeon, has already reported on its use in an earlier periodical. A description is offered of the conduct of the operation in the hope that others may use it and report on both its advantages and disadvantages and so perhaps help to clarify the status of the procedure.

Indications for the Use of the Combined Approach.—The combined approach will probably find its greatest usefulness in the resection of lesions of the middle third and lower third when the lesion does not involve the crura of the diaphragm. Adenocarcinoma of the cardia of the stomach with extension into the esophagus and with possible infiltrations into the left leaf of the diaphragm may be difficult if not impossible to remove safely through this combined approach.

Conduct of the Operation.—The operation is divided into two stages. These may be done consecutively on the same day or separated by an interval of seven to ten days. It is preferable, of course, to complete the operations on the same day.

First stage: An incision is made just to the left of the midline beginning at the xiphoid and extending below the umbilicus. The rectus muscle is split and the peritoneum opened. The peritoneal cavity is explored for evidences of metastases, particular attention being given to the liver, preaortic and paraesophagocardiac nodes, and the lymph nodes near the hilum of the spleen. Patients who present metastases to the liver are not considered suitable subjects for the complete resection. The gastrocolic ligament is taken down, the level of section being a few centimeters from the border of the right gastroepiploic artery. The individual vessels are secured with fine silk, and the dissection and ligation are carried around the greater curvature of the stomach dividing the left gastroepiploic artery and the vasa brevia passing to the spleen. The stomach is then turned upward and the left gastic artery doubly ligated as close to its origin as possible, thus leaving behind a sheath of vessels which may serve as collateral channels for blood being delivered from the right gastic artery. If large nodes are present about these vessels they will, of course, have to be resected with the specimen later in the procedure. The gastrohepatic mesentery is then divided to the diaphragm. If the left lobe of the liver obscures the field it is mobilized from the diaphragm by dividing the left suspensory ligament. This ligament is usually relatively avascular. The liver can then be retracted upward and free access to the esophagocardiac junction obtained. The peritoneal reflection from the diaphragm over the esophagus is severed after the anastomotic vessels which one commonly finds beneath this reflection are ligated. It is advisable to use silk (Lewis), for should one choose to allow seven to ten days to pass between

stages less reaction can be expected and therefore less likelihood of adhesion formation sufficient to interfere with delivery of the stomach into the chest. At this point the technique differs from that of Lewis. A point has been made of dividing the right crus of the diaphragm near its origin. It is felt that this division not only makes the blunt dissection from below of the lower two inches of the mediastinum easier but it allows one a larger space through which to maneuver the stomach during the thoracic stage of the operation. The diaphragm is also less likely to act as a partial obstruction to the vagotomized stomach at some later date. However, there are certain precautions to follow in dividing the crus which it may be worth while to mention. The origin of the thoracic duct from the cisterna chyli

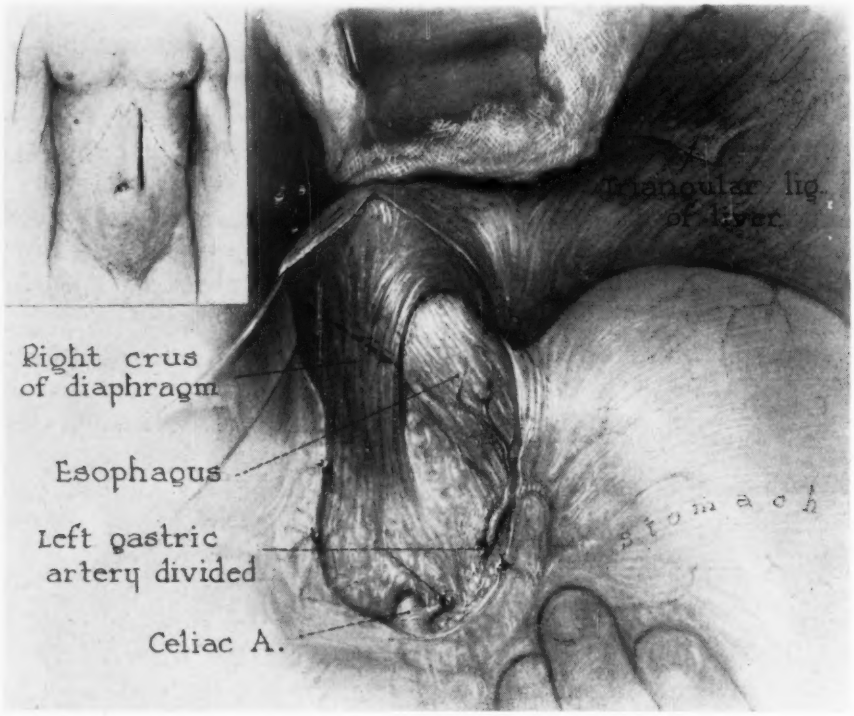

Fig. 1.—First stage (abdominal approach). The insert shows the approximate site and the extent of the abdominal incision. The large diagram indicates the approximate level of the section of the right crus after the stomach has been mobilized in preparation for delivery into the chest at the second stage.

takes place behind the right crus of the diaphragm and care should be exercised in cutting the muscle fibers so as not to injure this important structure. If blunt dissection is used on the cephaled surface of the crus, the soft tissues may be peeled away easily exposing the muscle fibers of the crus well back from its margin. The right inferior phrenic artery and its branches usually lie well back of the margin of the right crus but since the position is variable troublesome bleeding may occur when the crus is divided. Suture ligatures placed before the division is carried out may avoid any complication of this sort. When the esophagus has been freed from the mediastinum for

a distance of approximately two inches, the abdomen is closed. At this point a jejunostomy may be done for feeding purposes if the operator so desires to conduct the case. Fortunately in this operated series of twenty-one cases, patients in the large majority of instances could swallow liquids if given slowly and they had been prepared adequately by a high caloric fluid diet supplemented by drip feedings during the sleeping hours. For this reason there were not frequent occasions to use jejunostomy in preparation for resection. The closing of the abdomen completes the first stage. This procedure is attended by very little blood loss.

Second stage: The patient is turned over on the left side, the skin prepared, and the region about the seventh rib draped. Whether one selects the fifth, sixth, seventh, or eighth ribs depends a good deal on the level of the lesion as well as the height of the diaphragm. In general, that rib is selected whose neck is on a level two vertebrae above the upper border of the lesion as determined by x-ray examination. This, of course, is not accurate as the actual extent of the lesion may in some cases far exceed the apparent extension as determined by the roentgenologist. We can, however, transect the ribs above and below the resected one for further exposure as the case requires. The thorax is opened through the bed of the selected rib. The right lung is then gently decompressed and packed off medially. It may not be necessary to ligate and divide the azygos vein in lower third lesions but in all other cases it seems advisable. The mediastinal pleura is opened from a point three inches above the lesion down to the diaphragm and resectability is determined. Three types of local conditions have prevented resections in our hands. They are invasions of (1) the lung root, (2) the vertebral bodies, and (3) the aorta. When lesions lie behind the arch of the aorta, from the fifth to the third dorsal vertebrae, they are very likely, if adherent to the aorta, to be actually invading it. At lower levels, though they seemed to be adherent to it, careful and tedious dissection has usually freed them from this organ. This part of the dissection may prove to be very difficult if not impossible from the right thorax. Attempted dissection of a mass which seems to be invading the lung root has seemed more dangerous to us because of the very large venous channels whose position is often not exactly definable until an uncontrollable hemorrhage has occurred. When the mass has been freed from these important structures the resection can continue. There has been occasion when operating from the left side to have freed up the esophagus from the diaphragm up to the mass lying at the eighth or ninth dorsal vertebra, only to find the lesion not resectable. One need have little fear evidently for the viability of the esophagus so mobilized as there has been no subsequent perforation or mediastinal infection follow such procedures in this series. In general, it is better to determine resectability, when possible, before one has carried out the mobilization of the thoracic esophagus. When the mass has been freed from its contiguous structures and the esophagus carefully mobilized by blunt dissection and tireless hemostasis, the hand is passed down the

mediastinum into the abdomen and the stomach delivered into the chest. If adequate mobilization has been effected the stomach passes upward in nearly a straight line above the pylorus. The nodes about the cardia are dissected away from the stomach and left on the specimen. The stomach is then cut across just below the carioesophageal junction and turned in with three rows of sutures. The lower esophagus and mass are turned upward and the stomach is sutured to the esophagus behind the projected level

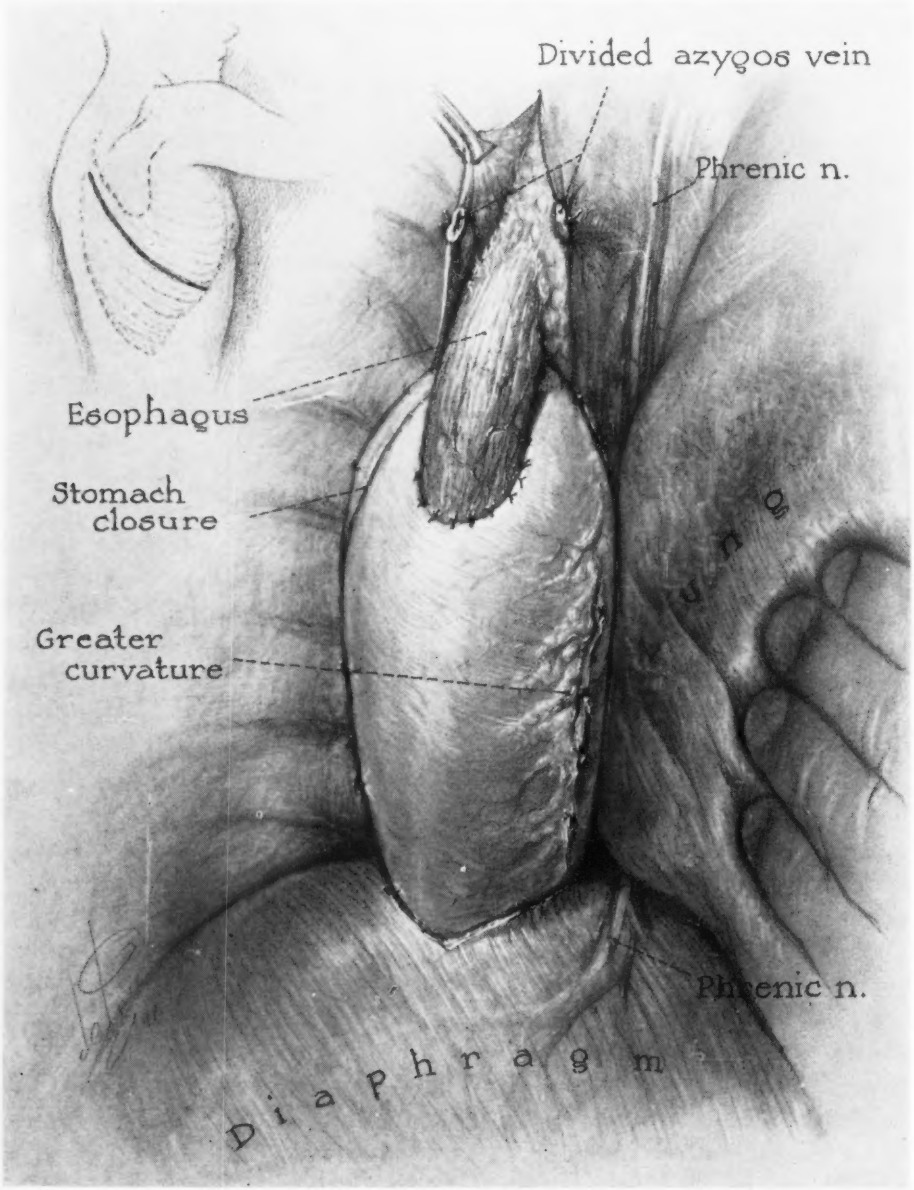

Fig. 2.—Second stage (thoracic approach). The relationship between the transposed stomach, the phrenic nerve, and the proximal esophagus as they lie in the right chest at the conclusion of the second stage.

of anastomosis. When one row of interrupted silk sutures has been tied the esophagus is transected using a clamp on the distal side only and the specimen is removed. It is believed that the esophagus should not be transected closer than two inches and preferably three inches proximal to the gross lesion. Others have noted the predilection for wide submucosal spread of this lesion. This is one outstanding advantage of the resection when done through the right side of the thorax. The level of the transection may be freely selected without substantially increasing the risk of the operative procedure. This is not usually the case when operating through the left side of the thorax. The retained esophagus should be handled as little as possible during these procedures. Interrupted silk is used in two rows for the anastomosis according to the technique of Sweet. The stomach is then sutured both to the diaphragm at the new hiatus and to the pleura to relieve strain on the anastomotic sutures. The pack is withdrawn and the lung reinflated. The thorax is closed with continous chromic catgut sutures in the pleurointercostal layer and with interrupted fine chromic sutures in the muscular layers. An intercostal drainage tube is used for forty-eight hours. At the conclusion of the skin closure the air is aspirated from the chest through this tube and 50,000 units of penicillin are instilled.

CASE 1 (No. 60181).—A 34-year-old man, a laborer, was admitted to the Institute complaining of progressive difficulty in swallowing of three months' duration and weight loss of twenty pounds in the same period. Roentgenologic examination revealed an ulcerating lesion of the esophagus 4 cm. long, lying at the junction of the middle and lower thirds of the esophagus with proximal dilatation of the esophagus and an old healed duodenal ulcer. Esophagoscopy on June 3, 1947, revealed an ulcerating obstructive lesion 35 cm. from the gum line. Biopsy showed some necrotic tissue along with chronic inflammatory tissue. No diagnosis of carcinoma was possible on the section. On July 1, after proper preparation, a combined left abdominal and right thoracic resection of the lower third of the esophagus and the upper portion of the stomach was carried out with intrathoracic esophagogastrostomy. Convalescence was uneventful. The patient was discharged from the hospital on July 23. Pathologic study disclosed an ulcerating lesion with firm induration extending through the entire wall of the esophagus producing almost complete obstruction. The sections, however, disclosed chronic inflammatory tissue with considerable scarring but no evidence of malignancy. This, therefore, was an old chronic benign ulcer of the lower esophagus with stenosis. No gastric mucosa was recognized in the specimen.

Comment.—At operation this lesion, except for a slight rubbery consisteney to palpation, appeared grossly similar to other lesions in this same location which proved malignant. The changes in the esophageal wall were not due to edema but were the result of long-standing chronic inflammation and presumably were largely permanent.

CASE 2 (No. 59865).—A 67-year-old white man, a laborer, was admitted to the Institute complaining of difficulty in swallowing and progressive weight loss (ten pounds) of four months' duration. X-ray studies disclosed an obstructing lesion of the esophagus 5 cm. in length at the junction of the middle and the lower third of the esophagus.

Esophagoscopy on April 29, 1947, revealed a fungating lesion 29 cm. below the gum line. This lesion on biopsy proved to be a typical squamous-cell carcinoma. Despite evidences of impaired renal function as revealed by the phenolsulfonphthalein test and Mosenthal concentration tests, it was felt that an operation was advisable. On June 10 a combined left abdominal and right thoracic resection was attempted. The first stage of the procedure was

completed, but after opening the thorax and mobilizing the distal esophagus the mass could not be freed from the left lung root. The stomach and lower esophagus were brought up into the right thorax easily through the widened hiatus. These viscera were returned to the abdominal cavity and the hiatus was repaired. The man developed increasing renal insufficiency on the third postoperative day and died in uremia seven days after exploration. At autopsy the cause of death was ascribed to advanced chronic interstitial nephritis with uremic ulcerations of the sigmoid and rectum. The stomach and lower esophagus gave evidence of being viable at the time of death despite the extensive mobilization of these organs during the first stage of the procedure.

ADDENDUM

Since acceptance of this paper for publication, five additional resections have been done by this method.

REFERENCES

1. Sweet, R.: Carcinoma of the Mid Thoracic Esophagus, Ann. Surg. 124: 653, 1946.
2. Garlock, John: Combined Abdomino-Thoracic Approach for Carcinoma of Cardia and Lower Esophagus, Surg., Gynec. & Obst. 83: 737, 1946.
3. Lewis, Ivor: The Surgical Treatment of Carcinoma of the Esophagus, Brit. J. Surg. 34: 18, 1946.

INTRAVENOUS CHOLECYSTOGRAPHY WITH TETRAIODOPHTHALIC FLUORESCEIN

GEORGE E. MOORE, M.D.,* AND MARCUS J. SMITH, M.D.,† MINNEAPOLIS, MINN.

(From the University of Minnesota Medical School)

SINCE Graham and his co-workers first reported the use of tetrabromophenolphthalein[1] and tetraiodophenolphthalein[2] for cholecystography, the latter dye has remained the most commonly used intravenous dye for this purpose. Its popularity as an oral contrast media for gall bladder examination, however, has been largely replaced by Priodax [beta-(3,5-diiodo-4-hydroxyphenyl)-alpha-phenylproprionic acid].

Many investigators have reported favorably the results obtained with Priodax (orally) as compared with those obtained with tetraiodophenolphthalein given either by the oral[3, 4] or intravenous route.[5] These reports have stressed the reduction in number and severity of toxic symptoms encountered when using Priodax.

The advantages of intravenous cholecystography are very real in some cases. A known quantity of dye is injected directly into the blood stream, the variable factor of intestinal absorption is circumvented, and the interval before the gall bladder can be visualized is shortened. For this reason it was thought that a report of an additional dye for intravenous cholecystography would be of interest.

Sodium tetraiodophthalic fluorescein was first employed at this clinic in an attempt to increase the radiopacity of certain intracranial lesions.[6] Since it was known that sodium fluorescein itself was largely excreted in the bile, incidental attempts were made to obtain cholecystograms. Thus, several of the first patients received much more dye than would be necessary for gall bladder visualization alone.

Iodinated fluorescein can be prepared in several ways.[7, 8] Iodine may be substituted directly into fluorescein, in which case the iodine is attached to the resorcinol part of the molecule. Erythrosin or "tetraiodoresorcinol-fluorescein" is an example of the resulting compounds. However, the parenteral use of erythrosin for producing radiopaque shadows is limited by its lack of solubility and its toxicity. In addition, its deep cherry red color is objectionable as the patient's skin would be deeply stained.

On the other hand, fluorescein compounds in which the iodine is substituted in the phthalic ring possess many clinical advantages. Their solubility is great, even with four iodine atoms introduced. The solubility of erythrosin is only

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about 10 per cent in water while tetraiodophthalic fluorescein is approximately 30 per cent soluble. Also, the iodophthalic compounds retain their fluorescence and, in addition, are lighter in color. Thus, they are less apt to cause an objectional staining of the skin.

The toxicity of erythrosin is much greater than that of tetraiodophthalic fluorescein. Preliminary toxicity studies indicate that the M.L.D./50 mice getting erythrosin is about 0.25 Gm. per kilogram, while that of tetraiodophthalic fluorescein is 0.45 Gm. per kilogram.

The pH of the di-sodium salt of tetraiodophthalic fluorescein is about 10. Although the monosodium salt has a more favorable pH, a rearrangement to form the di-sodium salt takes place with the application of heat and the remaining dye precipitates. Further addition of alkali is necessary to get all of the dye into the solution. The resulting solution of the di-sodium salt of tetraiodophthalic fluorescein is very stable and can be autoclaved. The final product contains 57.7 per cent iodine as compared with 55.2 per cent iodine in sodium tetraiodophenolphthalein.

Hexaiodofluorescein and octoiodofluorescein have been prepared, but their deep color, low solubility and toxicity negate their usefulness.

TECHNIQUE

In those instances, at the beginning of the study, where the amount of dye given intravenously was over 5 Gm., the dye was added to 5 per cent glucose solution and administered by a Murphy drip adjusted to allow the solution to run in over a half-hour period. Roentgenograms of the gall bladder were usually taken four to six hours after completion of the injection.

The final method worked out for gall bladder visualization consisted of the rapid intravenous injection of approximately 40 mg. of dye per kilogram of body weight, so that the total dose given adults ranged from 2 to 3 Gm. The dye solution was adjusted so that a convenient volume (15 c.c.) contained an individual dose. Direct intravenous injection was made within a period of one to two minutes.

Preparations were negligible. A light, fat-free breakfast was given on the morning of the examination; no other preparations were made. The first x-ray view was usually obtained two hours after the injection. If this showed a gall bladder shadow, a fatty meal was administered, and a second view (forty minutes later) of the gall bladder was obtained in order to show the contractility of the organ. If a poor or questionable shadow resulted, an additional roentgenogram was made in three hours. Oblique and upright views were obtained if necessary.

Selection of a two- to three-hour interval for gall bladder visualization was based upon studies made in which radioactive iodine was substituted in a similar dye and counts were made over the gall bladder with a Geiger counter. A marked increase in the counts over the gall bladder region was noted beginning forty-five minutes after injection.

TOXICITY

Originally, tetraiodophthalic fluorescein prepared by us frequently caused nausea and severe intestinal contractions, but later use of more purified samples* of the dye resulted in transient nausea in only two patients. There were no instances of vomiting nor did the patients complain of diarrhea which not infrequently follows the use of tetraiodophenolphthalein.

Three patients who received large amounts (9 to 10 Gm.) of tetraiodophthalic fluorescein over a prolonged period developed acute thrombophlebitis of the veins proximal to the site of injection. This complication, which was not encountered subsequently, was probably due to the long exposure of the intima to the alkaline dye solution (pH 10.0).

In two instances appreciable amounts of dye (estimated 30 c.c. of a 5 per cent solution) infiltrated into the subcutaneous tissue. Although local pain and some redness developed at the site of the infiltration, the transient inflammation regressed rapidly without therapy.

It was noted that all patients were tinted a light flesh-pink color by the dye and this color remained visible in the skin for several hours.

RESULTS

Twenty-two patients were examined by this method, some with biliary or gastric symptoms and some without (Table I). Two patients had pyloric obstruction, and intravenous cholecystography was necessary to visualize the gall bladder which previously could not be visualized after oral administration of Priodax. The results were (1) good visualization of the gall bladder in the majority of patients (Figs. 1 to 4), (2) nonvisualization of the gall bladder

TABLE I. INTRAVENOUS TETRAIODOPHTHALIC FLUORESCEIN

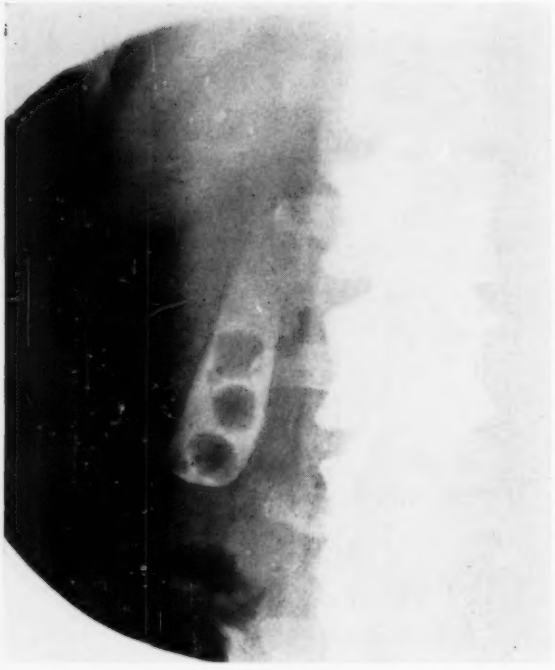
SUBJECT	AMOUNT (GM.)	TIME OF VISUALIZATION	DIAGNOSIS
A. W.*	10	3 hr.	Chronic cholecystitis
F. K.*	10	48 hr.	Chronic cholecystitis
E. K.*	9	10 hr.	Normal
R. S.*	8	No shadow	Absent gall bladder
M. H.*	7	5 hr.	Normal
O. J.*	6	15 min., 12 hr.	Normal
J. H.*	6	4 to 6 hr.	Normal
E. S.*	5	8 hr.	Normal
H. P.*	5	4 hr.	Normal
J. H.*	5	15 min.	Normal
A. T.	4	No shadow	Chronic cholecystis and cholelithiasis
M. T.	3	2½ to 3½ hr.	Normal
F. L.	2.5	2 to 4 hr.	Chronic cholecystitis
C. H.	2	1 hr.	Normal
M. K.	2	No shadow	Chronic cholecystitis
B. P.	2	2½ hr.	Chronic cholecystitis
J. E.	2	No shadow	Chronic cholecystitis
F. L.	2	3 to 4 hr.	Chronic cholecystitis
C. R.	2	No shadow	Chronic cholecystitis
E. S.	1.6	2 hr.	Chronic cholelithiasis

*Skull studies; cholecystography incidental.

*Supplied in part by Dr. D. L. Tabern, Abbott Laboratories, North Chicago, Ill.

Fig. 1.—Intravenous injection of 9 Gm. of tetraiodophthalic fluorescein; incidental x-ray view obtained at ten hours to demonstrate gall bladder filling.

Fig. 2.—Cholecystogram made four hours after the intravenous injection of 5 Gm. of tetraiodophthalic fluorescein.



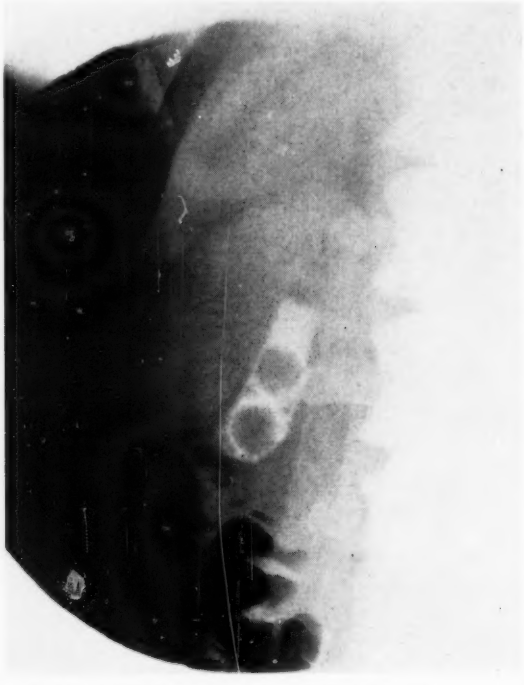


Fig. 3.—Rapid intravenous injection of 1.6 Gm. of dye. Roentgenogram made after two hours to demonstrate nonradiopaque calculi.

Fig. 4.—Same case as Fig. 3. Roentgenogram obtained forty-five minutes later, subsequent to fatty meal.

in four cases, and (3) nonvisualization of the common duct in a patient whose gall bladder had been removed previously. In the other four instances the gall bladder was assumed to be pathologic; this was correlated with clinical findings and was verified in two cases by subsequent surgery.

Further studies of tetraiodophthalic fluorescein and related dyes are in progress. It is hoped that the present technique can be varied so as to enable demonstration of the common duct itself. The possibility of administering the dye orally and subsequently studying several organ systems, is under consideration.

In addition, radioactive iodine has been substituted into iodinated fluorescein in order to measure more accurately the blood levels, concentration of the dye in the gall bladder, and rates and routes of excretion.

SUMMARY

Intravenous cholecystography utilizing tetraiodofluorescein is a simple, rapid, and nontoxic method. Dosage is approximately 40 mg. per kilogram. The optimum time for visualization appears to be two to three hours after injection. Subjective evaluation of the gall bladder shadows produced on the films shows densities comparable to those of tetraiodophenolphthalein. A minimum of preparation is necessary to obtain good cholecystograms.

The authors wish to express their appreciation to Dr. W. D. Armstrong, Department of Physiological Chemistry, for use of the facilities of his laboratory and to both him and Dr. Gerald Boyack, Department of Chemistry, for much helpful advice.

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METHOD OF MAKING TUBES OF POLYETHYLENE FILM FOR USE IN ANASTOMOSIS OF THE COMMON BILE DUCT, TRACHEA, AND PELVIC COLON

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THROUGHOUT the history of surgery a material has been sought which, although a foreign substance, could be used for surgical reconstruction of various organs and which would neither undergo change itself nor produce remote or local changes within the body. Of the many materials that have been tried, few have enjoyed continued popularity and use. Organic substances, such as animal membrane and rubber, produce more or less reaction and ultimately are resolved or become deteriorated. Certain metals and alloys, notably tantalum and vitallium, have been useful for some purposes. The usefulness of tantalum and vitallium is limited, however, because of certain physical characteristics, for example, their opacity to roentgen rays and their tendency to become overheated during application of short wave therapy to surrounding tissue, and because of rigidity and hardness in the case of vitallium and of high cost in the case of tantalum. Lucite, known also as acrylic, has proved to be a most satisfactory plastic material for many purposes. The disadvantages of lucite are that it is not flexible and that thin-walled articles are both difficult to make and brittle.

A variety of other plastic materials have been investigated recently. The polyvinyl resin series of plastics have a common disadvantage. They contain more or less of certain organic solvents, known as plasticizers, in order to make the plastic more flexible and translucent. Unfortunately, the plasticizers are slowly laked out of the plastic by many organic solvents, including those present in body fluids. Not only are plasticizers more or less irritating to tissue, but the plastic becomes opaque, hard, and rather brittle.

Another plastic which has received attention recently is polyethylene, or polythene. Polyethylene is formed by polymerization of ethylene and might be described as being ordinary paraffin which has been polymerized to a greater degree. Polyethylene is manufactured by a patented process and is then furnished to various manufacturers who convert the raw material to commercial products by an extrusion process. The extruded products are, as far as is known, either tubing, flat film, or rods.

Polyethylene is a material which some of us[1, 2] have found is superior to metallic or other plastic materials for surgical implantation in living tissue. A few experimental studies have been carried out in this laboratory, and others are in progress, which encourage us to believe that commercial polyethylene film and tubing will be useful in clinical surgery. Film has been permanently implanted to replace areas of dura or synovial membrane, and ventriculostomy

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tubes of polyethylene have been implanted permanently. Experimental studies have also suggested that polyethylene film be used in place of rubber for many temporary appliances, namely, for Penrose and rubber tissue drains, and to prevent adhesion of certain structures between stages of multiple stage operations.

As evidence accumulated in this laboratory that polyethylene was a superior material for implantation in tissue, a method of molding polyethylene into special forms became the object of a particular search. The immediate concern in this search was to make a tube for anastomosis of parts of the common bile duct, the hypothesis being that, because polyethylene (like its simpler form, ordinary paraffin) is not wetted by aqueous solutions, bile solids would not precipitate on the wall and occlude a tube of this material. It was soon recognized that commercially extruded tubing had a very limited use and that such tubing was not a suitable material out of which to mold objects. Commercial tubing is relatively thick walled; at molding temperatures the tubing contracts longitudinally, wall thickness increases, and the internal diameter decreases. When such tubing is drawn while it is at molding temperature, both thickness of the wall and internal diameter decrease. It was discovered also that it was impossible to weld flanges or ridges to commercial tubing without serious local encroachment of the lumen.

Eventually a method of making tubes and several other appliances out of polyethylene film was evolved. During the evolution of this method many peculiar properties of polyethylene came to be recognized.

PROPERTIES OF POLYETHYLENE

Polyethylene tubing or thick film is semitransparent and has a pearly gray color. It is tasteless, has a slippery "feel," and a very low coefficient of friction. It conducts heat very poorly and is an excellent electric insulator. Specific gravity is 0.92. Thin film of less than 0.005 inch (0.127 mm.) is transparent and colorless. Polyethylene softens and is therefore moldable at temperatures above 110° C. As polyethylene softens, it contracts in all planes, like glass. The degree to which contraction occurs varies with thickness, as indicated later. Between 60° and 110° C., polyethylene is slightly more pliable and soft than at lower temperatures, and molded or extruded objects tend to become distorted slightly in boiling water. It is less hard than lucite, but harder and much tougher than ordinary paraffin. Flexibility varies with thickness, thin film or thin-walled tubing being extremely flexible. Polyethylene does not crack or break and it can be cut easily with knife or scissors. It is elastic to bending and somewhat elastic to stretching force. The material, having a high tensile strength, can be drawn out considerably before it tears. It holds a suture very well. One of the most significant qualities of polyethylene is that its surface is not wetted by water or aqueous solutions.

Chemically, polyethylene is quite inert. It is unaffected by strong or weak acids or alkalies or powerful reagents such as fluorine gas. At temperatures of 60° C. or less it is unaffected by all known solvents. Pure polyethylene produces no tissue reaction, either inflammatory or foreign body.

TECHNIQUE OF MOLDING POLYETHYLENE TUBES

The underlying principle of this technique of making tubes is the fact that when polyethylene is heated to the point where it becomes soft, it shrinks. To take advantage of this characteristic, a sheet of thin film is wrapped around a form, which is a metal tube. When the film is heated and becomes soft, it not only fuses layer to layer, but the whole thickness of the wall shrinks tightly and uniformly to the metal tube, or form. In other words, the molding pressure or force is the shrinking force of the polyethylene itself. Such a method automatically creates a problem, that of removal of the polyethylene tube after it has fused and has shrunk tightly to the form. Obviously the form must be coated with a lubricant that will not be affected by heat, and the lubricant must also be covered by some material which will prevent incorporation of lubricant in the polyethylene during fusion. The latter material must be easily removable from the finished polyethylene tube.

The several steps in the technique are, accordingly, the coating of the form with a lubricant (soap), the covering of the lubricant with a material that can be removed from the finished tube (cellophane), the wrapping of the form with polyethylene film, the fusing of the film with heat, and the removal of the finished tube from the form.

The metal tube to be used as a form should have a uniform diameter and it should be perfectly round, free from dents and ridges, and smoothly polished. Its external diameter must be the same as the inside diameter of the polyethylene tube that is to be made; in other words, when one wishes to make a tube with a certain inside diameter, a form having an outside diameter of that measurement is selected.

Thin-walled brass tubes seem to make the best forms. This is probably because brass, which is a good conductor of heat, prevents overheating and burning of the polyethylene when too much heat is applied to one portion of the tube. A tube rather than a rod is used because the latter heats too slowly and because it is difficult to remove a polyethylene tube from a rod. Ordinarily it is best that the brass tubes be about a foot (30 cm.) long. Shorter tubes may be used if a handle is attached.

Steps in Making a Polyethylene Tube.—

1. *Coating of brass tube:* A film of a thick solution of a good grade hand soap is applied evenly to the brass tube and allowed to dry. All that portion of the tube about which film will later be wrapped must be covered by soap solution but it is well not to get soap on the rest of the tube. If there is soap on the uncovered portion of the tube the technician may get it on his fingers and thence on the polyethylene film. Soap on the film will spoil the tube when it is fused.

2. *Cellophane wrapping:* Next, a sheet of cellophane is wrapped tightly about the brass tube over the area covered by the soap film. The cellophane should be as wide as the length of tube covered by soap film, or at least 2 cm. wider than the length of polyethylene tube one contemplates making. Only enough cellophane to make two thicknesses is used. A satisfactory cellophane for this use is nonmoistureproof P. T. 300 (Du Pont). It is important that the film have no creases or wrinkles and that the edge be not curled.

3. *Polyethylene wrapping:* To make the *wall of the tube*, while the cellophane film is prevented from unrolling by holding it firmly between the thumb and finger tips, wrapping of the polyethylene film is started. The latter film will form the wall of the finished tube. The width of this film must be the same as the length of the tube to be made. In other words, to make a tube 5 cm. long, one uses a strip of film 5 cm. wide.

The thickness of the film used is most important. Film thicker than 0.004 inch (0.102 mm.) cannot be used because, during the process of heat fusing, it shrinks longitudinally, thus making a short and thick-walled tube. Film having a thickness of 0.003 to 0.004 inch (0.076 to 0.102 mm.) is best for tubes which are to have an internal diameter of 4 mm. or more. Because it is more easily rolled, 0.002 inch (0.051 mm.) film is preferred for tubes with an internal diameter of less than 4 mm. The number of turns of film wound in this step determines the thickness of the wall of the tube. Five turns, or five thicknesses of film, produce a tube with a thick but sufficiently rigid wall for most purposes.

After the desired number of turns of film have been wrapped and the unused strip of film has been cut off, the film is tightened by holding the handle of the brass tube in one hand and gripping the polyethylene-covered portion of the brass tube in the other hand. The two hands are then rotated in opposite directions, thus tightening the film. If the film is not tightly wrapped there will be air spaces between layers of film and, when the tube is heated, the air spaces will become bubbles. After the film has been tightened it is held in place by a tightly wound rubber band.

Thin ridges, wide bands, or flanges may be placed on the outside of the tube at any point. They are made by wrapping narrow strips of film at the point where the ridge, band, or flange is desired. Film for these structures is cut into long strips which, for the usual tube with an internal diameter of 4 mm. or more, are from 0.5 to 1 cm. wide. The wider the strip, the wider the band or the higher the ridge will be. The greater the number of turns or layers, the thicker the ridge or band will be.

A ridge is made by using a strip of film having a thickness of 0.005 inch or more. The best ridges are made with film of a thickness of 0.005 or 0.006 inch (0.127 or 0.152 mm.). Bands and flanges are made by use of film of the same thickness as that used to make the wall of the tube.

Winding strips of film on the tube is not difficult. Marks are made with the fingernail on the edge of the film used for the wall of the tube, these marks being made where the ridges or bands are desired. One end of the strip is slipped a short distance under the edge of the film of the tube wall and centered under the nail mark; then the wrapping is begun. When enough turns have been made to make the desired thickness of ridge or band, the unused portion of the strip is cut off and the wound strip held in place with a circular ligature. The ligature must be placed about the center of the band of film. Deknatel silk No. 000 or 0000 is a satisfactory ligature. Heavy cotton thread may be used for ridges of tubes to be used for temporary splints, for example, the two-piece tube for colon anastomosis after an anterior resection. If a radiopaque marker

is desired (polyethylene itself is nonradiopaque), a ligature of silver, tantalum, or other surgical wire suture is used.

4. *Fusing the tube:* The rubber band holding the film of the tube wall is removed. Loosening of the film will not now occur because it is held by the strips and their ligatures. If a band or ridge has not been placed near the end of the tube, or if there is a very long distance between ridges or bands, it is well to tie a heavy cotton ligature around the ends of the tube or in the middle of the long intervals. Such ties do not become imbedded in the tube wall and may be slipped or cut off the tube after it is fused.

The wrapped tube is fused by heating it to 110° to 115° C. In practice, it is far easier to govern the degree of heat by adjusting the distance between the source of heat and tube than by control of the source of heat. It is difficult to watch the fusing process closely in an oven and to remove the tube at the proper instant. Satisfactory sources of heat are an electric hot plate or a Bunsen burner covered by a wire and asbestos screen. If the latter source is used, the burner should be adjusted to give a gentle blue flame.

As the polyethylene-covered portion of the brass tube is held over the source of heat, usually about 2 inches (5 cm.) above the hot plate or wire and asbestos screen, it is rotated evenly. Within one minute, longer if the mass of tube is large, the polyethylene begins to become translucent. When it is completely translucent the tube is fused and must not be heated to a higher temperature. If only one end or portion of the tube is completely fused at this point, the brass tube is held tilted so that the finished end is farthest from the source of heat. As soon as all the polyethylene tube is fused it is cooled by passage of cold water through the brass tube.

If the tube has been designed to have bands or flanges and has, therefore, had several turns of thin film wound at the appropriate intervals, the strips remain flat during the fusing process. All that happens is that the several layers of each strip and the tube wall fuse together. A flange is made simply by pinching a band at some point on its circumference, while it is still soft, with a blunt pointed mosquito forceps.

If strips of thicker film (0.005 inch [0.127 mm.] or more) have been used to make ridges, a peculiar change takes place in the strips as they fuse. At first the edges of such strips thicken and ripple and, simultaneously, the two edges draw closer to the ligature which is midway between the edges. The edges continue to thicken and curl outward. A moment later the edges on each side of the ligature have met over the ligature and have fused evenly together. Fusion of the ridge is complete when these changes have occurred in all layers of the strip and the mass is homogeneous and translucent. The finished ridge is broadest at its base, where it is fused to the wall of the tube, and has a ligature buried in the middle of its mass.

5. *Removing the tube from its form:* Any heavy cotton ligatures which have been placed about the tube to keep the film tightly rolled during the fusion process are removed. Cellophane which protrudes beyond the ends of the fused tube is removed by pressing a knife against the edge of the tube while the

brass tube is rotated. Next the handle or free end of the brass tube is gripped firmly with one hand and the polyethylene tube with the other. Rubber gloves, or a piece of rubber dam held in each hand, prevent slipping and are a great help in this manipulation. As the hands are forcefully rotated in opposite directions the polyethylene tube along with its lining layer of cellophane becomes loose and can be slipped off the brass tube easily. The soap film both prevents cellophane from sticking to the brass form and lubricates the inner surface of the cellophane.

The lining layer of cellophane may be freed from the tube easily by running a blunt-pointed thin instrument between tube and cellophane. After it is freed the cellophane layer may be collapsed and extracted.

EXAMPLES OF MOLDED POLYETHYLENE TUBES AND APPLIANCES

A variety of molded polyethylene tubes have been made for experimental studies which are in progress in this laboratory. The following tubes are examples (Fig. 1).

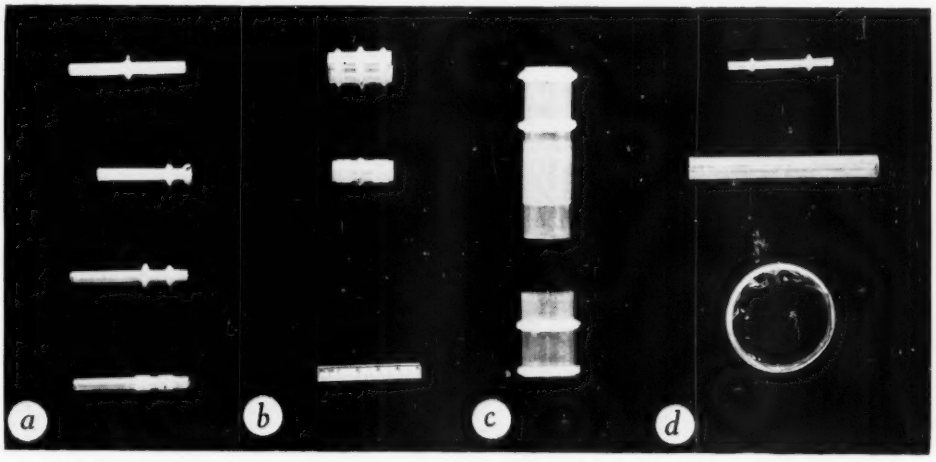

Fig. 1.—Examples of various types of molded polyethylene tubes and appliances. *a*, Tubes for use in the common bile duct. Four different types of tubes for use in common duct anastomosis are shown. *b*, Tubes for use in the trachea. The top tube is the type used for end-to-end anastomosis of parts of the trachea after resection of a portion of the trachea. The bottom tube is used for implantation in the trachea or a main bronchus. *c*, Tube for use in the anastomosis of the colon and rectum. The top piece of this two-piece tube is placed in the descending colon, the bottom piece in the rectum. After the tubes have been secured with purse-string sutures the proximal tube is inserted into the distal tube. *d*, Other tubes and appliances: top, a tube of very small diameter, with ridges; middle, a thin-walled tube of large diameter; bottom, a single layer of thin film with a ridge fused to its border.

Tubes for Use in the Common Bile Duct.—

For end-to-end anastomosis: A few tubes of this type have been used clinically. These are thin-walled tubes, their walls having five thicknesses of 0.004 inch (0.102 mm.) film, with an internal diameter of 4 mm. The tube is slightly flexible, which facilitates its insertion into the two limbs of the duct. Its conspicuous feature is a centrally placed ridge, one side of which has been flattened by pressure on the ridge while it was in the soft state. The other side of the ridge constitutes a tab, which will protrude through the duct wall at the

site of repair. A silk suture is passed with an ordinary surgical needle through the substance of the tab and anchored to the wall of the duct on either side of the tab. These tubes may be made in any length and may be cut to the desired size with scalpel or scissors at the time of operation.

For anastomosis of the common bile duct and the side of the jejunum or duodenum: This tube resembles the tube for end-to-end anastomosis of parts of the common duct except that it has no central ridge. Instead, it has a ridge at one end and another slightly larger ridge about 8 mm. behind the distal ridge. This collar-button-shaped end of the tube is inserted into a small hole in the side of the duodenum (or a loop of the upper part of the jejunum). The tube is placed so that the bowel wall is between the two ridges. An inverting purse-string suture closes the bowel about the tube. The other end of the tube, after the tube has been cut to the desired length, is inserted into the common duct. Interrupted silk sutures approximate the edge of the common duct to the duodenal or jejunal wall adjacent to the purse-string suture. One or two of these interrupted silk sutures include the outside ridge of the tube.

For anastomosis of the common duct and the end of a Y loop of jejunum: A variation of the tube last described has been constructed for use in a modification of the operation described by Allen, an operation in which anastomosis of the remnant of the common duct and the end of a Roux-Y loop of jejunum is established. In this operation the end of the jejunum is first inverted a short distance. Because at least 1 cm. of the jejunal wall has to be turned in, the two ridges of the collar-button-shaped end of this tube are placed about 1.5 cm. apart. Also, the end of the tube is allowed to project about 5 mm. beyond the terminal ridge. When the tube is in place the terminal ridge and projecting tip of tube should be inside the end of the blind loop and the other ridge should be close against the outside folded edge of the end of the Y loop. The free end of the tube lies in the common duct, and the edge of the common duct remnant is sutured to the edge of the bowel as in the previously described operation.

Tubes for Use in the Trachea and Bronchi.—

For end-to-end anastomosis after resection of a portion of the trachea: Such tubes have a diameter comparable to that of the trachea. At each end of the tube there is a ridge and in the middle there is a band with a small flange. In the anastomosis of parts of the trachea over this tube it is necessary to have the ridge at each end placed between tracheal rings. One of the interrupted silk sutures must transfix the flange in the center of the tube.

For implantation into the trachea or main bronchus: These tubes differ from the one just described only in that they have bands rather than ridges at each end, the bands serving to strengthen the tube where it would have its greatest tendency to collapse or become distorted. During the closure of the longitudinal incision in the posterior tracheal or bronchial membrane through which the tube is inserted, one of the interrupted silk sutures should transfix the flange.

All tracheal or bronchial tubes should be about twice as long as their diameters.

Temporary Tube for Use in Anastomosis of the Colon and Rectum After Resection of the Distal Part of the Colon.—This device is a two-piece tube, one piece of which fits inside of the other, making a snug sleeve union. Each piece of this tube has two ridges, one of which is at one end of the piece and the other 2 cm. from the end. The outside piece is short, being only about 3.5 or 4 cm. long. The inside piece is about 7 cm. long. After the colon has been resected and the crushing clamps removed from the rectum and proximal part of the colon, the inside piece of the tube is inserted into the end of the proximal part of the colon and the outside piece into the rectum through its open end, the ridge ends of both pieces being placed inside the bowel. Catgut purse-string sutures, which have been previously placed at the crushed edge of each portion of the bowel, are then tied and the inside, or proximal tube, is inserted into the distal tube. The ends of the purse-string sutures are tied together. An outer layer of interrupted silk sutures, which are easy to place because the tube within the bowel acts as a splint, completes the anastomosis.

After about one week, more or less, depending on the size of catgut used for the purse-string sutures, the tube is passed rectally, spontaneously. In the meantime all bowel content enters the tube proximal to the site of anastomosis and is conducted past the anastomosis through the inside tube. The double ridges of the tube on each side of the anastomosis protect against the passage of fecal content along the outside of the tube.

Other Special Tubes and Appliances.—It is possible to make tubes with small diameters and thin walls, with ridges or flanges, for use in blood vessels, brain ventricles, nasal sinuses, and so forth. The film which is 0.002 inch (0.051 mm.) thick is best for such tubes, the number of thicknesses depending on the desired thickness of the wall of the tube.

Tubes with walls only one layer thick can be made, although one side of the tube will be two layers thick where the film is overlapped. A couple of layers of cellophane are wound tightly over, as well as under, the film in this case. After the fusion operation the outside layer of cellophane must be peeled off carefully before the tube can be removed from the form.

By a variation of the technique described herein one can apply a polyethylene band or ridge to the edge of a bag of thin film. The band or ridge is wound about the edge of the bag near the end of a form, and the bag portion is covered by a metal cap. The metal cap is kept cool during the fusing process by covering it with a wet towel. If the metal cap were not kept cool, the bag beneath it would become soft and then would shrink and thicken.

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MANAGEMENT OF THE ILEOSIGMOIDAL FISTULA IN DIVERTICULITIS

Clinical Syndrome and Report of Four Cases

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IN GENERAL, the management of acute diverticulitis should be conservative even though the patient may appear acutely ill and, as not infrequently occurs, a partial to complete sigmoidal obstruction exists. The true or false diverticulum becomes inflamed because of inadequate drainage, probably due to an impaction of the diverticulum which irritates and causes ulceration of the body or neck of the sacculation. As in acute appendicitis, this inflammatory reaction may subside, but, unlike appendicitis, mortality figures reveal that the diverticulum does not so often perforate and cause general peritonitis and death. The inflammatory reaction of the diverticulum results in edema and induration of the sigmoid and of the mesosigmoid which encroaches upon the sigmoid lumen.

The patient with acute diverticulitis generally complains of lower abdominal pain and tenderness situated more to the left or in the midline, and not infrequently a mass can be felt. The pain may be cramping. Fever and leucocytosis are usually present. Nausea and vomiting, distention, and intestinal cramping and obstipation vary with the degree of obstruction of the colon and the extent of the inflammatory spread. A scout film may reveal dilated loops of small bowel, but more frequently reveals an enlarged colon or cecum. Low pressure barium enema studies may expose diverticula, narrowing of the involved segment, or complete obstruction. It is remarkable how frequently these patients improve after the gastrointestinal tract is placed at rest by instituting nasogastric or intestinal suction, hot abdominal packs, warm rectal irrigations, and antispasmodics. We are inclined to use penicillin if a tender mass is palpable and there is increased fever and leucocytosis.

Usually within two to four days the inflammatory reaction begins to subside and clinical improvement gradually follows. If obstruction has been present, gas and intestinal contents begin to slide through the narrowed segment of sigmoid. This improvement probably occurs when the neck of the inflamed diverticulum or diverticula opens by natural subsidence or pressure necrosis, and drainage from the sacculations is permitted. When the inflammation does not subside, pressure necrosis may cause the blocked diverticulum to perforate, resulting in a localized abscess or generalized peritonitis. When a localized inflammatory mass or abscess develops, loops of distal ileum usually become involved as part of the protective wall. Evidently at times the necrotizing action is sufficient to effect a break in the wall of the ileum with a resultant fistulous communication between the ileum and sigmoid. If the sigmoid has been obstructed and an ileosigmoid fistula has developed, the clinical picture is rather confusing. Abdominal cramps, active peristalsis, abdominal

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distention, and palpable bowel loops coexist in a patient who has frequency and urgency of stool. The picture is further clouded by variation of daily symptoms. One day the edema and inflammation in the region of the fistulous communication may be so severe as to cause partial to complete obstruction of both the involved sigmoid and the ileum. Then the edema obstructing the ileum may subside and frequent stools occur because of ileac contents emptying into the sigmoid, and at the same time cramping pains and signs of partial colon obstruction may exist because of edema and induration blocking the sigmoid. Again, the edema may block off the fistula and the ileac contents take their normal course to the colon only to meet obstruction in the sigmoid, in which event the clinical picture of sigmoid obstruction is again present. In these cases, the diagnosis of complicated ulcerative colitis, amebic or bacillary dysentery, or carcinoma of the sigmoid and rectum must be considered.

With obstruction threatening, barium should not be given by mouth. Also, one hesitates to give a barium enema but probably no harm will result if the radiologist is informed that an acute inflammatory condition possibly exists in the sigmoid and is impressed with the necessity of giving the barum enema very slowly and carefully and under low pressure. The barium enema may reveal a sigmoidal obstruction and some diffuse spread of the barium which is difficult to interpret. If not contraindicated by severe peritoneal reaction and abdominal tenderness, a proctoscopic examination will aid in eliminating the presence of low sigmoidal carcinoma or ulcerative colitis. At times, it is necessary to postpone proctoscopic examination for some days, but in any event it should be done before malignancy or ulcerative colitis is excluded. If the barium enema reveals a diverticulum, one may have a lead to the probable course of events and establish a diagnosis. However, because of the acuteness of symptoms, with fever, leucocytosis, and localized tenderness, one rightly tends to postpone a barium enema study and thus diagnosis is delayed. If no diverticulum is visible on the roentgenograms and there has been no previous diagnosis of diverticulosis, diagnosis of a perforating lesion with fistulous communication between the sigmoid and ileum is most difficult unless it is established that barium has entered the small intestine directly from the sigmoid. However, by correlating the events in the history just described with the abdominal examination, x-ray findings, and exclusion of rectal pathology by proctoscopic examination, the diagnosis can usually be made.

In the four cases presented here, two patients had associated pain in the upper abdomen and the diagnosis of gall bladder disease had been made elsewhere. In one a cholecystectomy had been done, and the patient stated that the surgeon had described a "strawberry-like gall bladder" to her. It is true that inflammation of pelvic organs or the pelvic colon may give rise to a peritonitis in the region of the liver and diaphragm, and one must be alert to this syndrome.

The syndrome of partial obstruction and urgency and frequency of stool occurs not too infrequently and many times leads to the incorrect diagnosis of inoperable rectal or sigmoidal carcinoma. Spontaneous recovery may occur after such a diagnosis, with credit directed to either the ingested medicine or a cultism followed.

When an inflammatory mass is present and diverticulosis exists, diverticulitis may be suspected. Malignancy may not be definitely excluded and an exploratory operation is recommended. Since the general condition of the patient is usually rather poor, the body fluid and chemical imbalance should be corrected and the serum proteins, red blood cells, and hemoglobin brought to a level compatible with undergoing a major surgical procedure. A nonabsorbable sulfonamide, sulfathaladine, having been our drug of choice lately, is prescribed in appropriate dosage. This is roughly calculated at 0.1 Gm. per kilogram weight for the initial dose, and the daily maintenance dose is similarly estimated, usually being about 1½ Gm., four times a day. This is continued for five days or until time of operation. The degree of active infection determines whether penicillin should be given, but in any event, penicillin is begun the day preceding operation. Nasogastric or nasointestinal suction is employed as indicated and is always instituted the evening before operation. Hot abdominal packs and warm rectal irrigations under low pressure may prove beneficial.

These four cases presented rather similar pictures at operation. A large inflammatory mass occupied the midabdomen at the level of the sacral promontory. From palpation and appearance, it is difficult to differentiate an inflammatory mass secondary to a perforated diverticulum of the sigmoid and adherent small bowel from a large infiltrating carcinoma of the sigmoid with small bowel involvement and a probable associated abscess. A one-stage procedure is preferable, but this was precluded in these four cases by the severe inflammatory reaction, density of adhesions, degree of edema, and the general condition of the patient.

In the presence of a fistula between the ileum and sigmoid, small bowel contents must be diverted from the inflammatory mass and sigmoid, or the symptoms of frequency and urgency of stool will continue. In these cases, a lateral anastomosis was made between the loops of ileum entering and leaving the inflammatory mass, thus permitting small bowel contents to by-pass the communicating fistula and inflammatory mass (Fig. 1). Consideration was given to dividing the loops leading to the tumor mass to be sure that ileae contents were completely diverted. This did not seem advisable because if the fistulous communication between the closed loops of ileum and the sigmoid blocked off, a blind loop of ileum would have resulted. From the experimental work of Stone, Bernheim, and Whipple,[8] Hartwell and Hoguet,[4] and Murphy and Brooks,[5] it was demonstrated thirty years ago that closed loops of ileum left within the abdomen resulted in toxic states, chemical imbalance, and death, as in true obstruction of the small bowel. The sigmoid is placed at rest by establishing a colostomy of the transverse colon.

One of these patients chose to keep the colostomy of the transverse colon. Usually she has a very slight amount of rectal discharge or a slight bowel movement once each day. She has no discomfort, eats normally, and has gained twenty-five pounds in weight.

The second patient elected to have the colostomy closed after barium enema studies revealed no further obstruction at the site of the previously blocked sigmoid. He has gained weight, elimination is normal, constipation has been

eliminated, and there is no history of frequent stools. X-ray studies do not reveal a communication between the sigmoid and ileum at this time.

The third patient insisted on closure of the colostomy. After one year, x-ray studies continued to show marked constriction of the sigmoid. At operation, the segment of sigmoid with attached ileal loops was resected. The remaining ends of ileum were closed and a primary anastomosis of the sigmoid was accomplished. The colostomy stoma was closed three weeks later.

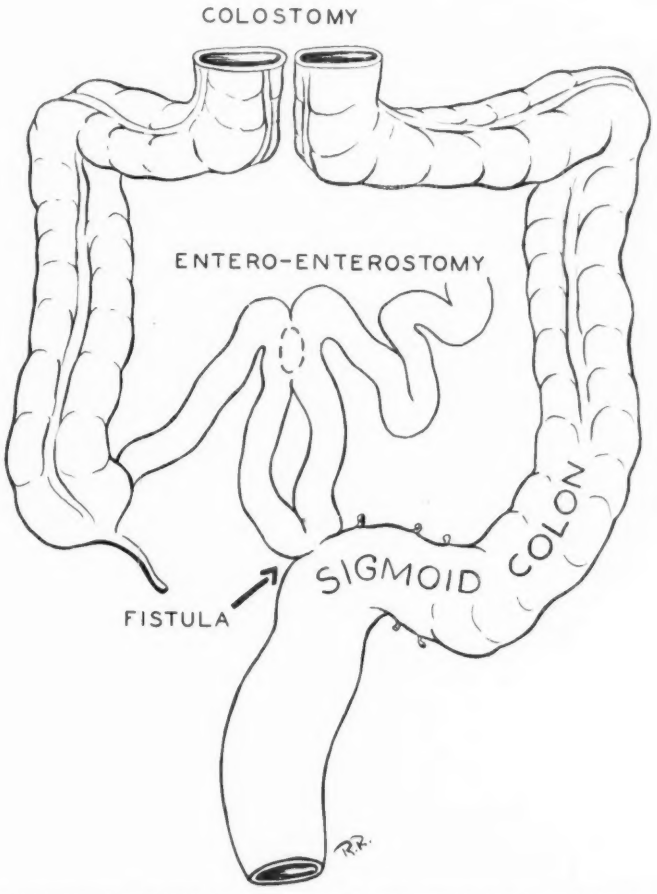

Fig. 1.—An enteroenterostomy short circuits bowel contents around the ileosigmoid fistula and inflammatory mass. The colostomy places the thickened, inflamed sigmoid with narrowed channel at rest.

The fourth patient, following the short-circuiting procedure and establishment of a colostomy of the transverse colon, gained twenty pounds in weight and refused further surgery, including closure of the colostomy. About fourteen months after the operation, she suddenly became quite anemic. A small mass was still palpable in the lower abdomen just to the left of the midline. Proctoscopic examination revealed negative findings, but when barium was given only a very small channel was present through the lower sigmoid region. Diverticula were still visible. Although the patient denied passage of blood per rectum or through the colostomy, the family finally divulged the fact that she had had several episodes of bleeding from the rectum and had passed black

fecal material through the colostomy. Because of the anemia, the patient was given a blood transfusion and surgery advised. At operation, the large inflammatory mass which was present at the original operation was only a small, hard, craggy mass; carcinomatous transplants were present on the peritoneum and metastatic nodules were palpable in the liver. No further surgery was attempted. This exemplifies what may be present in an inflammatory mass associated with diverticulitis.

SUMMARY

A report is made of four cases in which acute diverticulitis of the sigmoid had resulted in the formation of a fistulous communication between the sigmoid and a loop of ileum. The patients were very ill and presented a bizarre set of symptoms, suggesting intermittent bowel obstruction associated with urgency and frequency of stools. From the history, clinical observation, proctoscopic examination, and roentgenologic studies, a tentative diagnosis was established in each case, proved at operation, and immediate relief given by enteroenterostomy around the inflammatory mass and colostomy of the transverse colon. Of the four patients, one chose to keep the colostomy and have no further surgery; one was reoperated upon and only closure of the colostomy was done; the third did not desire to keep the colostomy and because the sigmoid continued to be constricted, resection of the sigmoid and short ileal loops was accomplished, followed by closure of the colostomy. The fourth patient later proved to have malignancy of the sigmoid associated with diverticulitis; the perforation could have been secondary to the diverticula or to the malignancy.

When a fistulous communication develops between the sigmoid and small bowel, the ileal fecal material should be prevented from entering the sigmoid and rectum in order to relieve the symptoms of diarrhea and rectal urgency. This is accomplished by enteroenterostomy. Complete diversion by section of the two loops should not be attempted because this might lead to establishment of blind bowel loops which are lethal. The sigmoidal obstruction is relieved and the inflammatory reacton of the diverticulitis of the sigmoid is permitted to subside by establishing a colostomy of the transverse colon. Further surgery at a later date is accomplished as indicated by the change in the pathologic condition and the wishes of the patient.

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TUMORS OF THE SMALL INTESTINE

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INTRODUCTION

IN CLINICAL investigations and classifications of tumors of the gastrointestinal tract, the emphasis has commonly been placed upon those new growths involving the stomach and the large bowel. This is understandable in view of the fact that the incidence of tumors at the extremities of the gastrointestinal tube is far greater than the incidence of those encountered in the interval small bowel segments. In terms of the known etiologic concepts and postulations on tumor growth it is perhaps not simple to explain the rarity of small bowel neoplastic processes. Certainly the concepts based upon embryologic rests cannot explain the low incidence of small bowel new growths as compared to the number met with in the stomach and large intestine. The various theorems with regard to chronic irritation may perhaps apply, in that the small bowel content is generally fluid as contrasted to semisolid and solid constituents of stomach and colon. Assuredly, there is a variety of materials secreted by, and eliminated into, the small intestine which can be classed as chemical irritants. The duodenum, for example, is constantly bathed in an abundant outflow of gastric juice, bile, pancreatic juice, and mucosal secretions; still, the incidence of duodenal malignancy is distinctly low.

In spite of the rarity of small bowel tumors, it is imperative that we exhaust all ingenuity in elaborating mechanisms referable to diagnosis and treatment. And this is so because we are confronted with the fact that malignancy of the small bowel is an extremely lethal disease.

ANALYSIS OF CASES

Incidence.—From the point of view of number of cases, our experience with tumors of the small intestine has been limited. After careful study of our files covering the last forty years, we have compiled a report on a total of 20 primary tumors of the small bowel; the clinical record on one of these cases is unavailable. Instances of ampullary tumors of the duodenum are omitted from this study because they are probably largely of duct origin. This number represents approximately 1 for every 3,300 surgical and autopsy specimens studied in this hospital. There are in our files records on 1,410 neoplasms of the gastrointestinal tract, from the esophagus, caudal. Thus, small bowel tumors have been encountered at the rate of 1 for every 71 neoplasms elsewhere in the gastrointestinal tract. In spite of this small total number it is interesting to note that 5 of the total of 20 were encountered during the year 1945.

In reviewing the literature on the subject of small bowel tumors, it is evident that our experience is the usual one, in that these tumors are conspicuous for their rarity.

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Distribution.—In the 19 cases available for clinical study, 13 malignant and 6 benign, the distribution between men and women was about equal in each group. The youngest patient having a malignant tumor was 35, the oldest 79 years of age. In the group having benign tumors, corresponding ages were 34 and 66 years. The average age incidence for those in the malignant group was 50 years, the benign group, 45 years. Growths of the small bowel probably follow the usual pattern of age distribution for neoplasms generally, in that the malignancies occur generally in the fifth and sixth decades, while the benign tumors are more likely to be encountered in the younger. Nevertheless, in the era of cancer consciousness, the trend is to disrespect more and more the traditional age limitations on clinical suspicion regarding malignant neoplasms. We must be even more on our guard inasmuch as, given the same histologic malignancy, it frequently will progress at a distinctly more rapid pace in a young than in an older person.

Duration of Symptoms.—In the malignant tumor group, there was no instance of an acute fulminating onset entirely unpreceded by previous complaints. The average duration of symptoms here was ten months, varying from one and one-half months to forty-eight months. Further breaking down of this small group revealed that 8 of the 13 patients had symptoms for only three months or less. In the group with benign tumors, symptoms varied from acute fulminating onset due to sudden intestinal obstruction, to thirty-six months. The average duration of symptoms for those patients with previous complaints was twenty-three months.

Clinical Symptoms and Signs.—In the malignant group the chief complaint was usually pain. This occurred in 9, or 70 per cent, of the 13 cases. The pain was usually described vaguely as indigestion with epigastric discomfort or more frequently as periumbilical or lower quadrant, intermittent aching. Six of the patients exhibited manifestations of bleeding; 4 complained of diarrhea, constipation, or intermittency of the two. Weight loss, anorexia, and cachexia were present in 11 of the 13 patients. On examination, 7 exhibited frankly detectable manifestations of obstruction, and in 5 instances there was a clinically palpable mass.

In the benign group of 6, there were 4 who complained of pain. This pain was usually described as lower quadrant in location, no matter which segment of the small bowel was involved. Diarrhea and/or constipation were noted in 3 instances, bleeding in only 1 instance. Systemic manifestations were complained of in only 1 case. One-half of the patients were obstructed, and in one-half a mass was palpable.

One cannot describe specific clinical patterns for the symptoms and signs of small bowel tumors. These vary from minor gastrointestinal distress with poor localization to a fulminating picture of acute, exasperating obstruction based on fairly sudden occlusion by an intraluminal mass or an acute intussusception. The dictum that any bizarre intestinal complaints, for which the usual methods of investigation offer no explanation must be further studied by pattern x-rays of the small intestine is upheld. One does not have the right to

discharge from observation a patient with persistent, unexplained gastrointestinal complaints without considering and studying the possibility of a small bowel lesion. Additionally, if bleeding is present the burden of proof is upon the physician to demonstrate its etiology, assuming that the statistically common gastroduodenal and large bowel pathologic entities have been excluded. It has been illustrated that chronic bleeding with a subjective ulcer syndrome in a patient without, and on rare occasions even with, x-ray manifestations of a gastroduodenal inflammatory lesion may be accountable to a small bowel tumor. In view of the frequently inconclusive x-ray findings of small bowel pathology, it is perhaps advisable to resort more frequently to exploratory laparotomy.

X-ray Findings.—In 6 instances of malignant, and in 3 of benign tumor cases, x-ray studies were not done, usually because the patient came in with acute obstruction or in extremis. In the 7 remaining malignant tumor cases, obstruction was demonstrable in 4 by radiologic examination. In 1 of these, the obstruction was interpreted as due to neoplasm; in the other 5 there was no postulation as to etiology. Two cases of the 7 studied by x-ray examination exhibited what were interpreted as filling defects due to tumor.

In the 3 benign tumors which were subjected to x-ray study, 1 was registered as a negative examination, 1 as a mechanical obstruction of the ileum, and 1 as a filling defect. Generally speaking, with regard to tumors of the small bowel, x-ray studies have been much less satisfactory than those of stomach and colon. Careful serial fluoroscopy and flash films of the small bowel following ingestion of a barium meal are essential, and interpretation by a competent radiologist is indispensable. Filling defects, changes in contour, localized paralysis and changes in intraluminal diameters are all exquisite points which must be left to the trained eye in all questionable cases. When an obvious extensive carcinomatous filling defect is present, more often than not the anatomic picture is one of a mass which has already extensively metastasized locally and distally. In a few instances, there is one pathognomonic x-ray sign corresponding to diffuse, infiltrative lymphosarcomatosis of a segment of bowel; in a small percentage of cases of bowel lymphosarcoma, barium studies will demonstrate a picture of a dilated, smooth aneurysmal-like sac, corresponding to bowel paralyzed by lymphosarcomatous infiltration. Frequently, a benign tumor will make itself known clinically and radiologically only when intussusception has occurred.

Pathology.—An analysis of the types of tumors encountered and of their respective locations and behavior with regard to intussusception is illustrated in Table I. Three neoplasms encountered in the duodenum were all malignant, 2 carcinomas and 1 malignant melanoma. There were none in the first portion of the duodenum. Two of the tumors were periampullary, and one was at the duodenojejunal junction. None of the tumors were intussuscepted. This complication did not occur with tumors of the duodenum due to the fixation and immobility of this bowel segment.

In the jejunum 6 tumors were malignant, including 5 carcinomas and 1 leiomyosarcoma, and 1 was benign. Four of the tumors were in the first portion of the jejunum, 2 in the second, and 1 in the third. Of the 6 malignant

TABLE I. DEMONSTRATING DISTRIBUTION, PATHOLOGIC TYPES, AND FREQUENCY OF INTUSSUSCEPTION IN THIS SERIES OF SMALL BOWEL TUMORS

SMALL BOWEL SEGMENT		PATHOLOGIC TYPES	TOTAL	MALIGNANT BENIGN		→ INTUSSUSCEPTION MALIGNANT BENIGN
Duodenum	I			Carcinoma	2	3 Malignant→ 0 Intussuscepted
				Melanosarcoma	1	
	II	Adenocarcinoma	2			
		Melanosarcoma				0 Benign ——→ 0 Intussuscepted
	III	Adenocarcinoma	1			
Jejunum	I	Polyp	4			
		Adenocarcinoma				
		Small-celled carcinoma		Carcinoma	5	
		Leiomyosarcoma		Leiomyosarcoma	1	6 Malignant→ 1 Intussuscepted
	II	Carcinoma	2			
		Adenocarcinoma		Polyp	1	1 Benign ——→ 1 Intussuscepted
	III	Adenocarcinoma	1			
Ileum	I	Submucous fibroma	2			
		Leiomyosarcoma		Carcinoma	1	
				Lymphosarcoma	1	
				Spindle-cell sarcoma	1	4 Malignant→ 2 Intussuscepted
				Leiomyosarcoma	1	
		Fibroma	2			
	II	Spindle-cell sarcoma				
		Submucous lipoma	6			
		Pedunculated fibroma		Fibroma	4	
				Lipoma	4	6 Benign ——→ 3 Intussuscepted
		Intramural fibroma		Leiomyoma	1	
	III	Leiomyoma				
		Adenocarcinoma				
		Lymphosarcoma				
			20			13 Malignant→ 3 Intussuscepted
						7 Benign ——→ 4 Intussuscepted

tumors, 1 produced an intussusception, and the single benign, tumor also was intussuscepted.

In the ileum, 4 malignant tumors were recorded: 1 each of carcinoma, lymphosarcoma, spindle-cell myosarcoma, and leiomyosarcoma; and 6 benign tumors, namely, 4 fibromas, 1 lipoma, and 1 benign leiomyoma. Two of the tumors were in the first portion of the ileum, 2 in the mid-portion, and 6 in the terminal, third. Of the 4 malignant tumors, 2 were complicated by intussusception, and 3 of the 6 benign tumors behaved similarly. In summation, one-half of the neoplasms were located at the extremities of the jejunoileal segment. This is also the statistical fact in large collected series of small bowel tumors, in that the majority are located near the beginning or the end of the small intestinal tube. Of the total 13 malignant tumors, only 3 were complicated by intussusception, whereas 4 of the total 7 benign tumors of the small bowel were intussuscepted.

The malignant neoplasms of epithelial origin were all of the adenocarcinomatous type. All more or less projected into the lumen, one constituting a large cauliflower-like mass. On microscopic examination all had infiltrated the muscularis but in only one was the serosa infiltrated and penetrated. At operation lymph node metastases were demonstrable in every case of adenocarcinoma. The lymph from the small intestine is collected in a subserous plexus and

drains to the nodes, most of which are situated close to the root of the mesentery. Only comparatively few and small nodes are found along the periphery of the small bowel mesentery at its insertion or in the intermediate zone. Unfortunately, only these latter can be included in resection of a bowel segment, the main nodes frequently being situated too close to the large branches of the mesenteric vessels to make the resection of this portion of the mesentery possible. The situation, therefore, differs unfavorably with that encountered in the lymph drainage of the large intestine and may account in some degree for the poor operative results in resection of small bowel for carcinoma.

The sarcomatous tumors apparently all arose from the smooth muscle, although all included such immature elements as may be considered to have been of fibrous connective tissue origin. They were represented by rather well-circumscribed, partly encapsulated masses, projecting into the lumen. They were attached to the deeper layers of the wall, the overlying mucosa usually being compressed, invaded, and partly ulcerated. Histologically two types could be differentiated. One comprised a very cellular growth uniformly composed of closely packed fusiform cells containing variously sized, often plump and hyperchromatic, nuclei. Mitotic figures were present and multinucleated tumor giant cells, areas of cystic degeneration, and necrosis were encountered here. This picture was present in one case in which a tumor tissue metastasis also was present in a regional lymph node. This patient died one and one-half years after operation, apparently of metastatic sarcomatosis. The other type, found in the remaining cases, presents a similar histologic picture which, however, is not uniformly found throughout the tumor but mainly in its central portions, the remainder being composed of newly formed, mature smooth muscle cells and fibers arranged in a rather orderly fashion as bundles or interlacing strands, supported by a well-differentiated fibrous connective tissue stroma. It seems fair to assume that the latter type represents a leiomyoma in which a sarcoma has arisen in contrast to the former where the malignant growth originated directly in the muscularis. It is thus, not surprising to find the clinical course of the latter to be benign, as these observations find their similarity in the uterus where one can often differentiate a sarcoma arising in the myometrium and one arising in a fibromyoma followed by similar clinical courses, respectively. In the case of lymphosarcoma the small bowel lesion was characteristic in every respect. It was situated at the predelection site, namely, just proximal to the ileocecal valve, where anatomically the lymphoid tissue of the mucosa is most abundant. Histologically it was of the lymphocytic type, containing only few "reticulum cells." Mitotic figures were absent. The neoplasm, apparently slow-growing, had only slightly invaded the muscularis but had completely destroyed and replaced the mucosa which was widely ulcerated. It formed several polypoid masses, the largest measuring 1.8 cm. in diameter and causing the intussusception. The regional lymph nodes were enlarged and extensively involved by lymphosarcoma.

The benign tumors of the connective tissue series encountered in the small intestine were all of their respective characteristic gross and histologic appearances.

The only benign tumor of epithelial origin was an adenomatous polyp in the jejunum; it measured 2.5 cm. in diameter and was attached to the mucosa by a narrow pedicle measuring 5 cm. in length. Due to the intussusception the tumor was extensively hemorrhagic.

Operative Procedure.—In the group of malignant tumors, 3 of the 13 patients were not operated upon: one was admitted in uremia, another in extremis, and a third had had a misdiagnoses of a retroperitoneal tumor and had been treated with deep x-ray therapy. Primary resection was done with immediate anastomosis in eight instances. In one case, a periampullary lesion in a patient who had been operated on twenty-six days before and at which time a cholecystectomy and a choledochotomy had been performed was biopsied at a subsequent laparotomy performed because of massive hemorrhage through the choledochotomy T-tube tract. Local excision with the cautery was resorted to in the case of the duodenal melanoma, adjacent to the empualla.

All 6 benign tumors were resected, side-to-side anastomosis being done in 5 cases and end-to-end in 1 case.

The treatment of lesions of the duodenum, malignancy in particular, is undergoing a revolutionary change. With the newer concepts of cholangiopancreaticoduodenal physiologic and surgical anatomy, as initially elaborated and practiced by Whipple over ten years ago, massive resections for previously regarded hopeless conditions are now entering the stage of practicability. In the jejunoileum, segmental resection including corresponding mesentery to its root is the obvious procedure. Nevertheless, the anatomic picture is usually one of distant dissemination at the time of celiotomy.

When an intussusception is encountered at operation, the situation is handled in the standard manner. If reduction cannot be easily accomplished because of the bulk of the tumor, the intussuscepted mass must be resected in toto. If inseparable adhesions between intussusceptum and intussuscipiens are present, the treatment is similar. Should the reduced intussusceptum exhibit alterations which lead one to suspect that mural vascular insufficiency is established, then one should include this region in the resection.

Recorded Results.—Regarding results of the 10 malignant tumors operated upon, there were 3 deaths attributed to the immediate postoperative period; 1 patient died on the first postoperative day of shock, a second on the fifth postoperative day of lobular pneumonia, and the third on the day of operation from shock following a heroic attempt which was made to resect the duodenojejunal junction and a large metastatic mass circumscribing the superior mesenteric artery. Four patients died of metastases three months, eighteen months, nineteen months and twenty months, respectively, following resection. One patient with diffuse ileocolic and rectal sarcomatosis was living and well eighteen months after extensive resection for an ileocecal intussusception secondary to a pedunculated ileal lymphosarcomatous tumor; this patient had been carried along very favorably with deep x-ray therapy. At the time of this writing, the only patients in this group living and entirely free of evidences of recurrence are the 2 in whom the tumor was a leiomyosarcoma. One is three years beyond

operation and the other, one and one-half years. Suffice to say, the 3 patients who were not operated upon died shortly after admission.

In the group with benign tumors one patient died six months after operation of metastases from an antecedent carcinoma of the cervix. Two died in the postoperative period of surgical complications; one, with a submucous fibroma of the ileum with intussusception, died on the third postoperative day of pneumonia. A second died suddenly on the fourth postoperative day following ileocecal resection for leiomyoma of the ileum with obstruction. The 3 remaining patients underwent uneventful recoveries and are surgically well.

None of the patients in the group having benign tumors died because of the intestinal neoplastic disease. On the other hand, all patients with carcinoma succumbed because of the intrinsic malignant disease. The outlook for lymphosarcoma of the small bowel is probably about the same as of carcinomas. In this group only those with leiomyosarcoma survived, establishing the fact that with the present treatment of malignancies of the small bowel, the over-all prognosis is extremely discouraging.

REVIEW OF THE LITERATURE

In the past several years, the literature has been fairly replete with reports on small bowel tumors. A review of a few of the more comprehensive surveys is in order at this juncture.

The impetus for study and classification of small bowel tumors was provided in exhaustive and painstaking surveys contributed by Raiford in 1932 and 1933. He reviewed in exquisite detail descriptions of 88 tumors of the small bowel recorded in the surgical pathology files at the Johns Hopkins Hospital. The small bowel tumors comprised 8.9 per cent of all gastrointestinal tumors. Of all benign gastrointestinal tumors 23.8 per cent and of all malignant tumors of the gastrointestinal tract 4.9 per cent were in the small bowel. In his cases, 37 per cent gave symptoms sufficient to warrant operation; 17 per cent had uncertain symptoms, were not operated upon, and the tumor was found at autopsy; 46 per cent had no symptoms, and the growth was discovered accidentally at autopsy.

Cave in 1932 reported on 14 small bowel tumors at Roosevelt Hospital. He classified the benign tumors into: lipomas, myomas, adenomas, carcinoids, hemangiomas, fibromas, pancreatic rests, and cysts. Carcinoma was the most common of the malignant tumors. He emphasized the investigation of early, nondescript, mild gastrointestinal complaints.

Duodenal malignancies are dealt with in a recent publication by Dixon and associates. They demonstrated that diagnosis here is somewhat facilitated in contrast to similar lesions in the jejunum and ileum because of the changes in clinical physiology produced by expanding lesions compressing or occluding the duodenum, the pancreatic system, or the biliary system. Consequently, roentgenologic examination was relied upon earlier, as patients were driven to medical consultation by manifestations of obstruction, bleeding, jaundice, or pain. Roentgenologic evidence of obstruction in the second or third portions of

the duodenum makes it expedient to consider neoplasm as a diagnostic possibility. They discussed recent advances in operative approaches, and cited a case of duodenal carcinoma which was resected two years after it had been identified at a previous operation. They concluded that the prognosis is better with duodenal neoplasm than with neoplasm in the jejunoileal segments because earlier symptoms are elaborated, as the mass impinges upon adjacent stomach or upon either or both of the two ducts.

In 1936, Doub and Jones reported on primary small intestinal malignancies. Malignant tumors of the duodenum are reviewed in detail, and clinical diagnoses classified according to position, namely, supraampullary tumors resulting in pyloric obstruction, periampullary tumors yielding obstructive jaundice, and infra-ampullary tumors resulting in obstruction with bile vomitus. Carcinomas are described in terms of constitutional symptoms and the regional symptoms secondary to (1) acute obstruction, usually due to an intussusception, and (2) gradual occlusion by the tumor with slow, progressive obstruction. Sarcoma of the ileum and jejunum is discussed and the occasionally seen pathognomonic x-ray picture of localized, aneurysmal dilatation of a small segment of bowel due to difluse mural infiltration is reviewed. These authors quoted Mumey as noting that 65 per cent of intestinal sarcomas are encountered in the small bowel.

Cameron gave an excellent, concise review of the clinical pathology of primary malignancies of the jejunum and ileum. He reported on 4 of his own cases and on 196 accumulated from the literature. He concluded that carcinomas and sarcomas of the small bowel are nearly equal in incidence and that malignant carcinoids comprise 6.5 per cent; that mechanical obstruction is caused by 80 per cent of carcinomas and by over 50 per cent of sarcomas; and that diagnosis is frequently impossible in nonobstructive cases. His assimilated figures indicated that in one-sixth of the cases a clinical diagnosis is correctly made; two-thirds of the cases are operable, the operative mortality being 30 per cent and five-year survival less than 10 per cent.

In a review of intestinal lymphosarcomas, Usher and Dixon offered stasties on prognosis for small bowel lymphosarcomas. They found that the average survival was nine months as contrasted to two years for lymphosarcomas of the rectum and eight years for lymphosarcomas of the cecum. All but 2 of the 19 patients operated upon for lymphosarcomas of the small bowel died of recurrence within a year. They reported on 50 cases of intestinal lymphocarcoma with 38 per cent located in the small bowel. Reticulum cell sarcoma and malignant lymphocytoma (small round-cell sarcoma) are distinguished.

Melanoma of the small intestine is usually regarded as a pathologic rarity. Herbut and Manges reported on 5 cases and noted 25 others in the literature. They reviewed convincing evidence that melanoma of the small bowel is perhaps always a metastatic tumor, even when the primary tumor is not evident, as in our case, because often the fact of a previously removed small skin lesion is not made known or permission to retain the eyes at post-mortem examination is unobtainable.

X-ray diagnosis of small intestinal malignancies was reviewed by Swenson on 120 cases. Usually the patient did not present himself until obstructive symptoms had occurred. X-ray qualities were reviewed in terms of size and shape of the small bowel lumen, contour and pattern of its walls, and the effect of the tumor on the motility of the bowel. Serial half-hour roentgenograms were stressed. In the discussion of this review, Ross Golden pointed out that in the differential diagnosis, the lesion produced by a carcinoma or carcinoid is usually short, 4 to 6 cm. in length, whereas an inflammatory lesion is usually considerably longer.

Gastrointestinal smooth muscle tumors were reviewed by Golden and Stout in an excellent analysis of the literature of the entire subject of leiomyoma of the gastrointestinal tract. They demonstrated the paradox of the classification of these tumors into benign and malignant, illustrating that frequently, poorly differentiated histologically malignant tumors do not behave so clinically, while occasionally, infiltration and metastases are subsequently exhibited by a histologically well-differentiated tumor. They also discussed the confusion encountered in differentiating these tumors from other connective tissue tumors, particularly the neurilemmonas.

A word might also be added concerning carcinoid tumors. Many reports in the literature regard these "basal cell" tumors of the intestinal wall as entirely benign. This is not always the case as several reports are available of unquestioned carcinoids of the small intestine, the appendix, or the cecum, which have metastasized to regional nodes and/or to the liver.

Thirty-five cases of benign, small intestinal tumors at the Mayo Clinic were reported in 1933 by Rankin and Newell. In order of frequency, these included adenomas, myomas, fibromas, lipomas, hemangiomas, submucous cystadenomas, adenomyomas, and subserous osteochondromas. Eighteen of the cases included symptoms, and in 17, the tumor was encountered incidentally at laparotomy. Symptoms were essentially those secondary to intussusception, progressive intraluminal obstruction, and hemorrhage. They observed that the most common single cause of intussusception in adults is a benign tumor of the small intestine.

Regarding lipomas of the gastrointestinal tract, there have been few significant contributions to the subject since the classical review on *The Submucous Lipoma of the Gastro-intestinal Tract*, by Stetten in 1909. Schottenfeld reviewed the literature in 1943, with emphasis on the subject of intussusception, and added 6 of his own cases.

The subject of obscure gastrointestinal hemorrhage has lately and rightfully been receiving more attention in the literature. Baker and Halley reported 2 cases of small intestinal neurofibroma with long-standing recurrent episodes of tarry stools, in the presence of otherwise good health. In each case, suspicion of ulcer existed, but the instituted ulcer management was followed by a recurrence of the bleeding. They further give a concise review of the interrelationships of fibroma, neurofibroma, and leiomyofibroma, and demonstrated the difficulty in histologically distinguishing these at times.

Smith and associates reported 2 cases of small intestinal tumor as a cause of recurrent melena at the Mayo Clinic. They called attention to the fact that in cases of ulcer type pain, a demonstrable deformity in the duodenal bulb, and a history of melena, two lesions may be present and the melena may be from a coexistent tumor of the ileum or jejunum. Difficulties of x-ray diagnosis are pointed out. The expense and time involved in small bowel serial x-ray views sometimes are great, and, at that, not all lesions are by any means demonstrable. However, such examination is indicated when no lesion is found in the rest of the gastrointestinal tract to explain bleeding or where it appears probable that the known lesion is not the source of the bleeding. They offered interesting stastics: in a review of the cases of bleeding there were 266 sources of bleeding found in the stomach or duodenum for every one found in the small intestine beyond the duodenal bulb. A relatively small number of instances of melena are the result of tumors of the jejunum or ileum, but the incidence of bleeding from tumors in this area is very high.

Segal and his co-workers also wrote on lesions of the small intestine producing massive hemorrhage. They noted that the combination of postprandial pain and melena being produced by lesions in the small intestine beyond the duodenum has not been stressed in the literature. They reported on 3 patients with such lesions, 2 of whom had repeated hospital admissions, each time being treated for bleeding duodenal ulcer. They reviewed 2 other similar cases in the literature and suggested in detail added diagnostic measures. T. E. Jones, in the discussion with the article, made a plea for early exploratory operation in all cases of exsanguinating hemorrhage, even though the x-ray findings are consistently negative.

CASE REPORTS

All cases are graphically analyzed in Table II. Two of these are noted here in more detail. The one, a case of leiomyosarcoma of the ileum with chronic intussusception in a young adult, illustrates pertinent features in regard to the behavior of this group of tumors from the point of view of clinical and radiologic diagnosis, treatment, and result. The second, a case of spontaneous ileocolostomy secondary to a primary carcinoma of the ileum, demonstrates the late stage at which the patient is frequently seen in consultation for the initial time and additionally exhibits the guarded prognosis which carcinoma of the small intestine bears.

CASE 1.—T. K., a 33-year old white man, a clerk, was admitted to the hospital with the complaint of mild abdominal "rumblings" and short episodes of crampy pain for two months. For five days prior to admission the pain was noted more frequently, was accompanied by some nausea, and the patient had vomited several times during the four days prior to admission and three times on the day of admission. He claimed to be able to pass flatus freely. There was no history of diarrhea or constipation; no bloody or tarry stools; no jaundice. The remainder of the history was noncontributory. On physical examination the patient did not appear chronically or acutely ill. Pulse and temperature were normal. Examination of the abdomen revealed entirely negative findings except for minimal tenderness just below and to the left of the umbilicus. No mass was palpable. Auscultatory sounds were normal. Rectal examination was negative except for the presence of a sentinel hemorrhoid. The white blood count was 9,000, with a normal distribution. The patient was observed

carefully during the next forty-eight hours, during which he seemed to experience a complete recession on the complaints; flatus and stool were passed. On the third day crampy pain recurred and on physical examination there was no distention, but for the first time there was noted a loop-type succussion splash on rocking the patient and on direct auscultation. No visible peristaltic waves were demonstrable and sounds were not excessive in any of the abdominal quadrants. A gastrointestinal series taken at this time exhibited several loops of small bowel which were perceptibly distended. At twenty-four hours the barium was distributed irregularly from the cecum to the sigmoid. The findings were interpreted as characteristic of a partial mechanical small bowel obstruction.

Fig. 1.—Intussusception secondary to leiomyosarcoma of ileum. The obstructed loop of ileum in the left upper quadrant is visualized. The blank area between this and the arrow near the midline corresponds to the intussuscepted segment, and here the region of faint distribution of barium peripherally represents the interval between the intussusceptum and intussuscipiens.

Laparotomy was performed five days following admission. A small bowel obstruction was present. This was caused by an intussuscepted 18 cm. segment of upper ileum. The intussusceptum was readily reduced by gentle taxis. All involved bowel and mesentery appeared viable. The apex of the intussusceptum was formed by a pedunculated, firm, intraluminal tumor the size of a small prune; there was dimpling of the serosa corresponding to the tumor. Two enlarged hard lymph nodes were noted at the base of the mesentery in the drainage field of the tumor. A block resection of a generous segment of ileum with a wedge of corresponding mesentery extending to its root was done, and a side-to-side enteroenterostomy performed. The patient made an uneventful recovery and prior to discharge two weeks after operation a repeat gastrointestinal series was interpreted as: "there is still some dilatation of one of the loops of small intestine, apparently proximal to the enteroenterostomy; the amount of distension is considerably less marked than on the previous examination."

The tumor was a pedunculated leiomyosarcoma; the enlarged nodes included in the resection were extensively inflamed but contained no metastatic deposits.

TABLE II. TUMORS OF THE SMALL BOWEL—ANALYSIS OF THE CASES IN THIS SERIES

CASE	AGE-SEX	DURATION OF SYMPTOMS	PRESENTING SYMPTOMS	BLEEDING	PALPABLE MASS	OBSTRUCTION	X-RAY FINDINGS	PREOPERATIVE DIAGNOSIS	PATHOLOGY AT OPERATION OR AUTOPSY	OPERATIVE PROCEDURE	OUTCOME OR FOLLOW-UP
1. 1909	36 F	36 mo.	Crampy lower abdominal pain, recurring prolapse of the rectum	No	Yes	No	——	Polyp of sigmoid with intestinal inversion	Submucous lipoma of lower ileum with chronic ileocecal intussusception to splenic flexure	Partial reduction, resection of fixed intussuscepted mass, and primary anastomosis	Uneventful recovery; well when last seen 3 mo. later
2. 1917	52 M	19 mo.	Epigastric pain, distention; anorexia, weight loss	No	No	No	Filling defect of cecum suspicious of malignancy	Carcinoma of cecum	Pedunculated fibroma of lower ileum with intussusception	Resection of lower ileum and end-to-side ileocolostomy	Convalescence uneventful
3. 1918	— M	——	——	—	—	—	——	——	Fibroma of ileum	——	——
4. 1918	34 M	24 mo.	Bleeding, diarrhea	Yes	Yes	No	GI series and barium enema negative	?	Intramural fibroma of power ileum	Resection of ileum and side-to-side ileocolostomy	Uneventful recovery
5. 1927	43 M	10 hr.	Upper abdominal crampy pain, vomiting	No	Yes	Yes	——	Intussusception or volvulus	Submucous fibroma of upper ileum with irreducible intussusception	Resection of involved ileum and side-to-side anastomosis	Died on the third P.O. day of fulminating bronchopneumonia
6. 1928	42 F	3 mo.	Weight loss, right-sided abdominal pain	Yes	No	Yes	Dilatation of lower loops of ileum	Tuberculous salpingo-oophoritis	Spindle-cell sarcoma of middle ileum with partial obstruction and node metastases	Resection of ileum and Murphy button, end-to-end anastomosis	Died 1½ yr. later, probably of metastatic sarcomatosis
1930	51 F	6 weeks	Weight loss,	No	No	Yes	——	?	Adenocarci-	——	A chronic ne-

1930 7.	51 F	6 weeks	Weight loss, cachexia, vomiting	No	No	Yes	——	?	Adenocarcinoma of duodenojejunal junction with partial obstruction (autopsy)	——	A chronic nephritic, died 5 days after admission in uremia
8. 1932	66 F	7 weeks	Diarrhea, crampy lower abdominal pain, vomiting, weight loss	No	No	Yes	Mechnical obstruction of ileum in right lower quadrant	Intestinal obstruction (gastrectomy 15 yr. before and operation for strangulated hernia 14 yr. previously)	Leiomyoma of lower ileum with obstruction	Ileocecal resection and side-to-side ileocolostomy	Died suddenly on the fourth P.O. day
9. 1934	37 F	24 mo.	Anorexia, weight loss, "upset" stomach	No	No	No	——	Miliary tuberculosis, tuberculous meningitis	Carcinoma of middle jejunum (autopsy)	——	Died one day after admission in extremis, of cachexia and amyloidosis
10. 1935	58 M	3 mo.	Chills, fever, and jaundice	No	No	No	——	Cholecystitis, cholelithiasis, and choledocholithiasis	Adenocarcinoma of duodenum distal to ampulla	Duodenotomy and biopsy second produre done 26 days following cholecystectomy and choledocholithotomy: severe hemorrhage on 25th day	Died in shock on first P.O. day
11. 1936	79 M	3 mo.	Constipation, coffee-ground vomitus, melena; anorexia, weight loss, periumbilical pain	Yes	Yes	No	GI series and barium enema negative for obstructive lesion	Retroperitoneal tumor	Small-celled carcinoma of upper jejunum with node metastases	—— (Treated with radiation)	Died of bronchopneumonia 3 mo. after admission
12. 1936	45 M	12 mo.	Crampy lower abdominal pain, anorexia, severe pain for 4 days	No	Yes	No	——	Appendical abscess	Adenocarcinoma of lower ileum with omental and peritoneal metastases	Resection of lower ileum and single large metastasis; side-to-side anastomosis	Died of bronchopneumonia on the fifth P.O. day

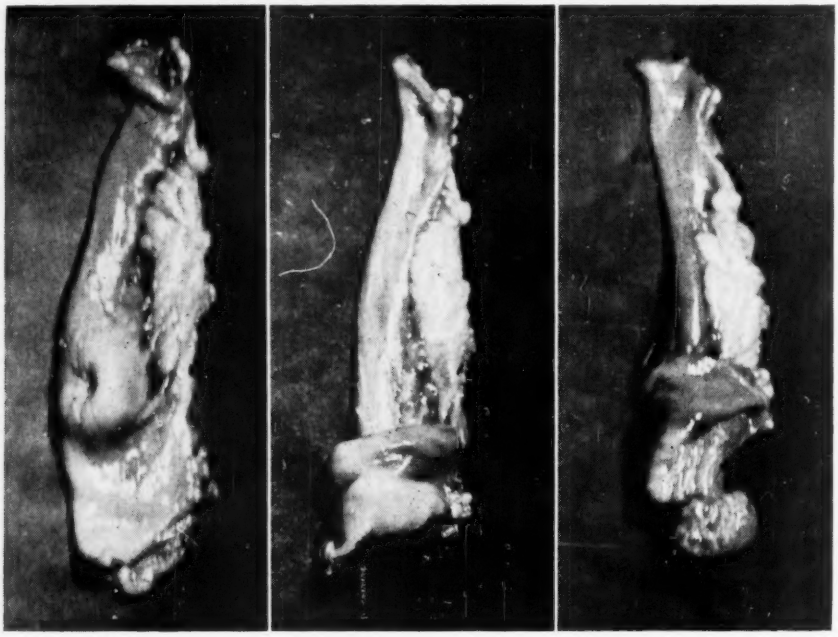
TABLE II—CONT'D

CASE	AGE-SEX	DURATION OF SYMPTOMS	PRESENTING SYMPTOMS	BLEEDING	PALPABLE MASS	OBSTRUCTION	X-RAY FINDINGS	PREOPERATIVE DIAGNOSIS	PATHOLOGY AT OPERATION OR AUTOPSY	OPERATIVE PROCEDURE	OUTCOME OR FOLLOW-UP
13. 1942	56 F	6 weeks	Crampy abdominal pain, constipation, nausea and vomiting	No	No	Yes	Stomach, duodenal, and jejunal dilatation indicating complete obstruction 6-8 cm. from ligament of Treitz	Intestinal obstruction	Pedunculated leiomyosarcoma of upper jejunum with intussusception	Reduction of intussusception, resection of jejunum, and side-to-side anastomosis	Uneventful recovery and well after 3 yr.
14. 1943	37 F	4 hr.	Sudden, severe abdominal pain in upper quadrants; prostration and shock	No	No	Yes	—	Volvulus of small bowel	Polyp of jejunum with nonreducible intussusception	Resection of intussusceptED mass and side-to-side anastomosis	Died 6 mo. later of metastases from antecedent carcinoma of cervix
15. 1944	59 M	2 mo.	Sporadic vomiting, tarry stools, weight loss	Yes	No	Yes	Partial obstruction of midjejunum with a filling defect, probably neoplasm	Jejunal obstruction secondary to tumor	Carcinoma of midjejunum with obstruction and node metastases	Resection of jejunum and side-to-side anastomosis	Died of liver metastases 20 mo. later
16. 1945	44 M	48 mo.	Rectal bleeding, diarrhea, weight loss, crampy lower abdominal pain	Yes	Yes	Yes	—	Intestinal obstruction secondary to intraabdominal lymphosarcoma (known lymphosarcoma of peripheral nodes for 4½ yr.)	Ileocecal intussusception to the midtransverse colon secondary to polypoid lymphosarcomatous masses of ileum, and lymphosarcomatosis of colon and of mesenteric nodes	Resection of reduced intussusception because of infarction of latter, and side-to-side ileocolostomy	Patient has received three courses of x-ray therapy and is clinically without evidence of disease 18 mo. P.O.

17. 1945	55 F	2 mo.	Watery diarrhea, weight loss, anorexia	Yes	No	No	Irregular appearance of the lower descending colon with some of the barium enema passing medially into a loop of small intestine	Enterocolostomy, secondary to malignancy, probably of descending colon	Adenocarcinoma of lower jejunum with direct extension to descending colon and ulcerating through latter; mesenteric node metastases	Mobilization of ileocolostomy tumor mass, division of jejunal limbs with side-to-side enteroenterostomy, and obstructive resection of descending colon plus attached ileal limbs	Died of carcinomatosis 17 mo. postresection
18. 1945	33 M	2 mo.	Crampy upper abdominal pain	No	No	Yes	Findings characteristic of a partial mechanical obstruction of the small bowel	Small bowel obstruction, possibly secondary to Meckel's diverticulum	Leiomyosarcoma of upper ileum with intussusception	Reduction of intussusception, resection of ileum; and side-to-side anastomosis	No evidence of recurrence 14 mo. P.O.
19. 1945	64 M	16 mo.	Pain in the right upper quadrant, fullness in stomach after meals, weight loss	Yes	Yes	Yes	Filling defects in duodenum characteristic of a malignant neoplasm . . . (re-examination of a "negative" GI series done 9 mo. before showed a then unrecognized, early lesion here)	Primary carcinoma of the duodenum	Adenocarcinoma of third portion of the duodenum with mesenteric and peripancreatic metastases	Resection of third portion of duodenum and upper jejunum, and end-to-end duodenojejunostomy (Murphy button)	Died of shock and infarction of small bowel on day of operation
20. 1945	35 F	12 mo.	Pain in right upper quadrant, jaundice, weight loss	No	Yes	No	——	Cholecystitis, cholelithiasis, and choledocholithiasis	Malignant melanoma of second portion of duodenum with metastatic extension into ampulla	Cautery excision of tumor and curetting of common duct, cholecystogastrostomy, and T-tube drainage of common duct	Died 3 mo. P.O., of liver metastases

The preoperative x-ray views of this patient are exhibited in Fig. 1. The interval between the small bowel loop on the left and that on the right corresponds to the intussuscepted segment; in retrospect, it is understood that the thin peripheral distribution of the barium here corresponds to the (potential) space between intussusceptum and intussuscipiens. Serial pictures of the resected gross specimen are demonstrated in Fig. 2; the mechanism of intussusception is re-enacted in these photographs.

Small bowel barium studies done in our tumor clinic follow-up six months later exhibited essentially no pathologic changes.



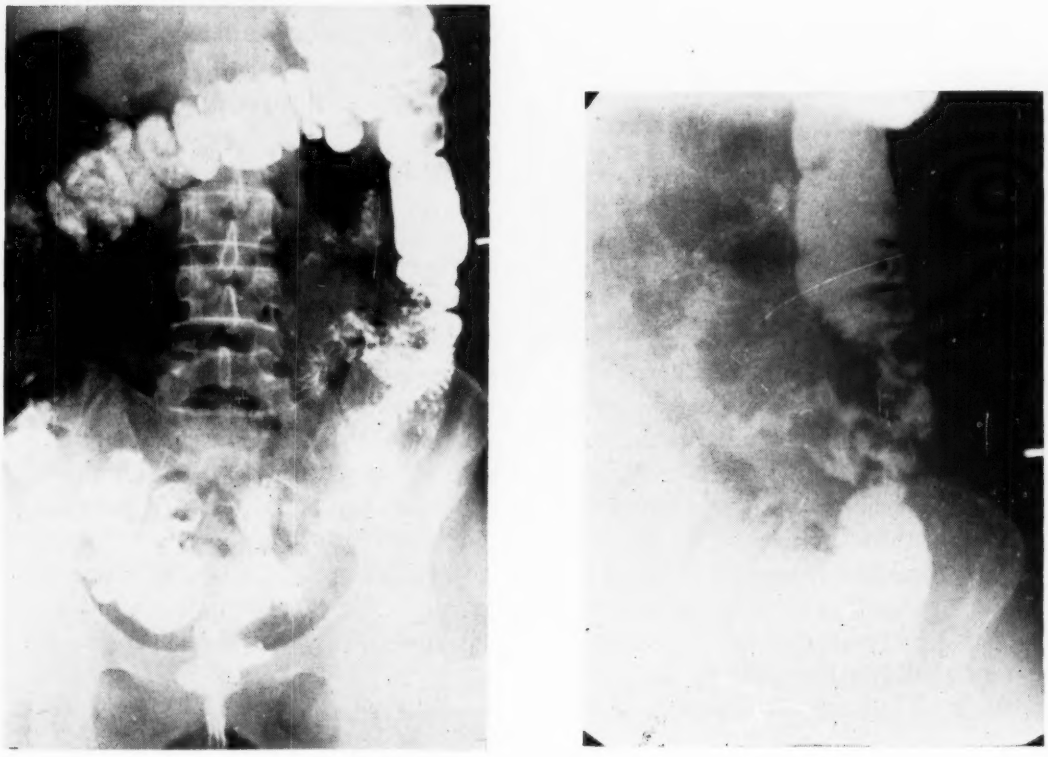
A. *B.* *C.*

Fig. 2.—Reproduction of mechanism of intussusception in patient with leiomyosarcoma of the ileum. *A*, The resected specimen; note serosal dimpling. *B*, The tumor intussuscepting into the adjacent caudad cuff of ileum. *C*, Further progression showing the pedunculated tumor forming the head of the intussusceptum.

CASE 2.—A 55-year-old white woman, a domestic worker, was admitted to the hospital with the complaint of watery diarrhea for two months. Five to seven stools were passed daily. There was no nausea, no vomiting, no abdominal pain. No blood had been noticed in the stool. Findings from the system review were negative except for dyspnea on exertion. There was a twenty pound weight loss during the illness. On physical examination the patient appeared chronically ill. Pulse and temperature were normal. There was a systolic murmur at the cardiac apex. Examination of the abdomen was entirely negative except for minimal distention. On admission the hemoglobin was 60 per cent; red blood cells, 3.1 million; white blood cells, 7,600 with normal differential. Stools were negative for ova and parasites but contained, on chemical examination, a trace of blood. Stool culture: revealed Escherichia coli. X-ray barium enema studies taken some time after admission were interpreted as showing an irregular appearance of the lower descending colon, suggestive of malignancy, with some of the barium passing medially through the bowel wall and entering a loop of small intestine; enterocolostomy, possibly secondary to neoplasm. The patient was transferred to the surgical service and was prepared for operation with a course of sulfasuxidine, multiple transfusions and infusions, and parenteral vitamin therapy. Hemoglobin, blood chloride, and blood plasma protein were elevated to values permitting operation. An attempt to pass a Miller-Abbott tube preoperatively was unsuccessful because the tube knotted in the stomach following instillation of 4 c.c. of mercury into the balloon.

Exploration was carried out on the patient three weeks after admission. In the region of the descending colon there was a tumor mass involving four limbs of intestine, namely, two of lower ileum and one each of upper and lower descending colon. The entire mass was mobilized. The ideal afferent and efferent constituents were divided, each at a considerable distance from the mass. Side-to-side ileo-ileostomy was then done. The sigmoid and left colon with attached ileal limbs were then further mobilized and delivered, and a Rankin obstructive resection was performed. The patient made an uneventful convalescence, the proximal clamp having been removed fifty-four hours postoperatively.

Careful examination of the resected specimen gave all evidences of the lesion having been a primary carcinoma of the lower ileum which had become adherent to and ulcerated through adjacent lower descending colon serosa and muscularis, and in one small region had disrupted colon mucosa resulting in the enterocolostomy.



A. *B.*

Fig. 3 *A* and *B*.—Barium enema studies on patient with adenocarcinoma of lower ileum, with recent ulceration into descending colon. X-ray films demonstrate the ileocolostomy.

A spur-crushing clamp was applied on the twelfth postoperative day. An indurated area appeared at the margin of the colostomy during the third week. Although the biopsy of this was interpreted as "carcinomatous infiltration," the indurated area soon was transformed into smooth glistening mucosa of pouting colostomy stoma. Seven weeks following the resection extraperitoneal closure of the colostomy was done. A barium enema two weeks thereafter showed some irregularity near the junction of the descending colon and sigmoid, probably representing scarring at the site of the colostomy; the impression was of normal function of the colon following sigmoid resection.

The patient was followed very carefully in our tumor clinic. Within four months she had gained twenty pounds and was working actively. Barium enema studies at this time showed smoothening out of the anastomotic line with no suggestion of recurrence. One year

following initial resection the patient was carefully examined in routine checkup and was found to be entirely well. However, seventeen months postresection the patient returned from a position in Maine with the history of weakness, nausea, cough, and weight loss for one month. Findings were reflective of disseminated peritoneal and cervical lymph node carcinomatosis. The patient was admitted to the hospital and died of the malignant condition within two months of onset of symptoms of recurrence and within eighteen months following resection.

The original barium enema studies on this patient are demonstrated in Fig. 3.

SUMMARY AND CONCLUSIONS

A careful survey has been made of all the material on tumors of the small bowel in the past forty years in a large voluntary hospital. Representative works in the literature on the subject are reviewed. Two cases of malignancy of the small bowel, one a leiomyosarcoma of the ileum in a young adult and the other an adenocarcinoma of the ileum ulcerating into the descending colon, are presented in detail to demonstrate the problems which malignant neoplasms of the small bowel involve.

This study on a small group of cases substantiates the experiences of others who have encountered and treated neoplasms in these portions of the gastrointestinal tract. Tumors of the small bowel are conspicuous in their rarity. But concerning the benign group, it may be said that there exists no more evasive a group of lesions; with regard to the malignant group, there are few malignant neoplasms which are more lethal, at least as applied to the carcinomas. Therefore, these lesions must be kept in mind by the clinician and the surgeon in the analysis of any vague gastrointestinal complaints in any age group or in the investigation of obscure gastrointestinal bleeding. A particular symptom complex simply does not exist. Additionally, even the carefully planned radiologic investigation may be inconclusive in establishing a diagnostic interpretation leading to the conviction of the existence of a small intestinal neoplasm. Therefore, because of these latter facts and because of the present status of minimal risk involved in elective abdominal surgery, one is led to feel that laparotomy should be resorted to more frequently in those instances where exhaustive diagnostic studies leave one in doubt.

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PANCREATIC CYST

Internal Drainage Utilizing The Roux Principle

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ADAMS and Nishijima‡ recently reviewed the literature on pancreatic cysts and presented the experiences of the Lahey Clinic with nine cases encountered there in the last twenty years. Six of these cases were pseudocysts two were papillary cystodenocarcinoma, and one was a hemorrhagic cyst.

They prefer internal drainage to marsupialization. This is accomplished by carrying a loop of jejunum through the transverse mesocolon and anastomosing the jejunum to the cyst wall and then they perform a jejunojejunostomy to divert the intestinal stream.

Utilization of the Roux principle seems a more logical way of accomplishing this as it gives us a long arm which drains the pancreatic cyst. The peristaltic waves in this arm will hinder, if not prevent, the contamination of the cyst by food particles in a greater percentage of cases than can be expected from the loop techinque.

This principle was utilized in the treatment in the following case.

Mr. S. was seen at the Rhode Island Hospital in April, 1947. He gave a history of having had symptoms of gall bladder disease for years. An acute cholecystitis in 1946 was treated by cholecystectomy, June 14, 1946. During the months following this operation the patient suffered from three attacks of acute pancreatitis, all of which subsided, but he noted some swelling in the epigastrium. The swelling increased gradually until at the time of admission it was quite pronounced (see Fig. 1).

He had no desire for food and was easily upset by many types of food. There was a sensation of pressure in the upper abdomen. There had been no jaundice or clay-colored stools. There was constant backache.

Except for the visible, fixed, and nontender mass in the epigastrium extending over into the left hypochondrium, there were no significant findings except for the roentgenogram, taken April 17, 1947, which showed the shadow of a large round soft tissue mass in the upper midabdomen probably due to a pancreatic cyst. The anterior and lower margins of the mass were sharply delineated but the upper margins were obscured by the density of the liver and other soft tissue structures. No visible calcification was seen within the mass. Renal shadows were normal in size, position, and outline. Psoas sheath and other soft tissue structures appeared normal. The colon was displaced downward and forward by the mass. There were no signs of intestinal obstruction.

The diagnosis of pancreatic cyst was obvious and surgery was accepted by the patient. On April 21, 1947, operation was performed. Internal drainage of the pancreatic cyst was carried out using the Roux principle. The cyst was quite high in the abdominal cavity, and because of this the old right subcostal incision was used as a means of entering the abdomen. The incision was carried across the midline and part of the left rectus muscle and sheath were

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†Surgeon, Out Patient Department, Rhode Island Hospital.
‡Adams, R., and Nishijima, R. A.: Surg., Gynec. & Obst. 83: 181, 1946.

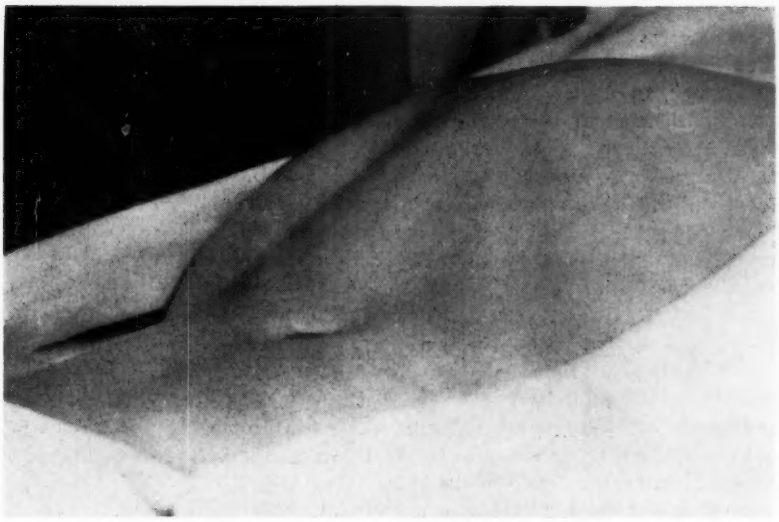

Fig. 1.—Photograph showing marked fullness in the upper abdomen.

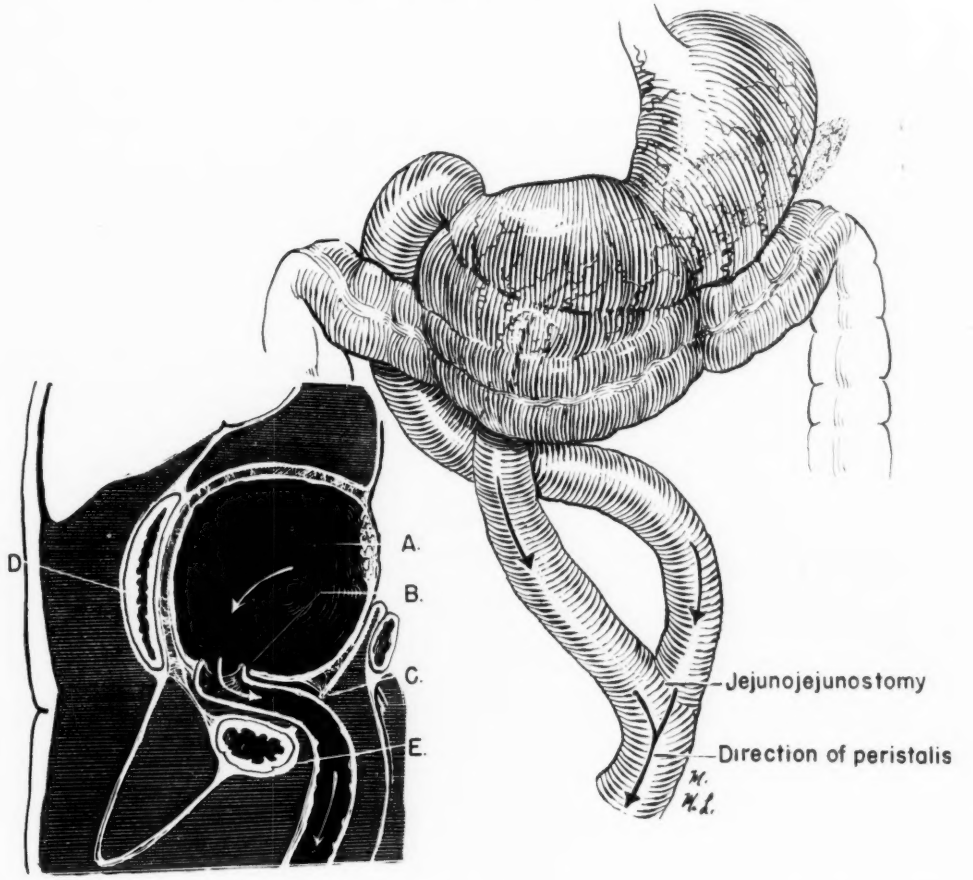

Fig. 2.—Drawing illustrating anatomic features of operation. *A*, Cavity of pancreatic cyst; *B*, stoma at junction of cyst and jejunum; *C*, jejunum going through transverse mesocolon; *D*, stomach; and *E*, transverse colon.

incised so as to obtain adequate exposure. The stomach was flattened out. The cyst was very large and measured approximately six to eight inches in diameter. It was very tense. The cyst was then dissected free from the posterior wall of the stomach, after it had been approached through an opening in the gastrocolic omentum, thus exposing enough of the cyst wall as was needed in performing the anastomosis. The cyst was then opened, and approximately 1100 c.c. of dark brown fluid were removed by suction. The ligament of Treitz was identified. Approximately six inches below this point the jejunum was transected. The distal end was carried through an avascular portion of the transverse mesocolon, and an open anastomosis was carried out between the cyst and open end of the jejunum using outer rows of C-silk mattress suture and an inner row of No. 00 extra hard chromic with a lock stitch posteriorly and a Connell anteriorly. The anastomosis seemed to be quite firm and satisfactory. The cut end of the proximal jejunum was then sutured to the distal limb of the jejunum approximately six inches below the point of anastomosis of the jejunum to the cyst. This was an end-to-side anastomosis, using the open technique and mattress sutures of C-silk on the outer layer and No. 00 chromic extra hard on the inner layer. The wound was then closed in layers using No. 00 double continuous in the peritoneum and also posterior fascia, No. 0 chromic mattress in the fascia and muscle, No. 0 chromic interrupted in the fascia, and interrupted silk in the skin. (See Fig. 2.)

The convalescence in this case was uneventful. The patient was out of bed on the second day and home on the eighth day.

During the first twenty-four hours gravity drainage with a Levine tube was instituted. Nothing was given by mouth for forty-eight hours, and then sips of water were allowed for the next forty-eight hours. Following this a fourth day Balfour diet was used with the usual progression. On the seventh day the patient tolerated a soft diet well and he was kept on this for another week. After this period a regular house diet was advocated. Six weeks after the operation the patient had already gained twelve pounds. He enjoyed the food and had no symptoms of any kind.

The enlargement noted in the upper abdomen disappeared on the operating table and did not recur.

It is obvious that no one can draw any conclusions from the results obtained in this case, but it is felt that this case can be used as further evidence that internal dainage of pseudo cysts of the pancreas is the procedure of choice over marsupialization with all its hazards of prolonged drainage, skin irritation, etc.

Moreover, adoption of the Roux principle to drain pancreatic cysts is advanced as being preferable to the use of a loop of jejunum with a jejunojejunostomy.

SUMMARY

1. Internal drainage of pancreatic cysts is advocated.

2. The Roux principle seems to offer more chance of eliminating contamination of the cyst than does the use of a loop of jejunum with or without jejunojejunostomy.

3. A patient successfully treated by utilizing the Roux principle is reported upon.

CHRONIC INFLAMMATORY INTESTINAL OBSTRUCTION DUE TO ENTEROBIUS VERMICULARIS

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INTESTINAL obstruction as a result of infestation with worms has occasionally been reported with *Ascaris lumbricoides* usually the offending agent and with most of the cases occurring in children. The indictment of other worms as a cause of intestinal obstruction is rare. Many authors in their reviews of the problems involved in bowel obstruction do not mention *Enterobius vermicularis* as an etiologic agent.

E. vermicularis is usually and rightly regarded as a relatively innocuous inhabitant of the human intestinal tract producing as its main symptoms a pruritus ani and an occasional secondary infection of the perineum from scratching. The ova are ingested orally and are carried into the small intestine where copulation of the male and female occurs. The males succumb and the females with their ova migrate into the large intestine and out through the anus where the ova are deposited. A mild catarrhal inflammation of the intestinal mucosa produced by these worms has been reported by many authors. Manson-Bahr* has found that mature worms may penetrate the mucosa, become encysted in the submucosa of the small intestine or appendix, and may give rise to inflammation in these areas.

Encystment of the adult female in the serosa of the sigmoid colon was found in the case being reported. A chronic intestinal obstruction secondary to inflammatory and fibrotic changes resulted. Such cases are infrequent in occurrence and interesting when their paucity is contrasted to the usually high rate of human infestation by this nematode within the United States.

CASE REPORT

The patient was a 56-year-old white man, an elevator operator, who was admitted to the hospital with complaints of diarrhea, hiccup, and abdominal distention. He stated that the present illness had started about three weeks before admission with crampy abdominal pain and a moderately severe diarrhea consisting of about eight stools a day. The stools were liquid in character and did not contain blood or purulent material. This episode of diarrhea lasted for about three days, and was followed by the intermittent passage of semisolid and liquid stools for the following 2½ weeks. The patient had a liquid stool just after admission to the hospital. Periodic attacks of hiccup developed four days prior to admission and lasted as such for three days, when they became particularly persistent. Six days before entrance to the hospital he had a sudden severe attack of lower abdominal pain which lasted four hours

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*Manson-Bahr, P.: Tropical Diseases, Baltimore, 1945, Williams & Wilkins Company, 920 pp.

and gradually disappeared without recurrence. Three days later anorexia and abdominal distention gradually developed but nausea and vomiting were not present during this period except that on the day of entrance to the hospital breakfast was vomited.

A past history of gastrointestinal complaint, severe illnesses, and venereal infection was not obtained. Surgical procedures had not been performed previously. The patient had served as a soldier in France during World War I but otherwise had always lived in the United States.

Physical examination revealed a seriously ill, slightly obese, white man with anxious countenance and a persistent hiccup. Discoloration of the skin and mucous membranes was not present. The temperature was 102° F., the pulse rate 101 per minute, the respiratory rate 24 per minute, and the blood pressure 122/80, measured in millimeters of mercury. Physical findings were essentially within normal limits except for the abdomen. This was markedly and symmetrically distended but visible peristalsis was not seen. Muscular spasm and tenderness were completely absent, and enlarged solid viscera and abdominal masses were not felt. Auscultation revealed the presence of peristaltic motion through tinkling and splashing sounds over the left portion of the abdomen. Inguinal or femoral hernia was not found. The prostate was normal to digital examination and masses were not felt in the rectum or rectosigmoid. Blood was not seen on the examining finger.

A scout roentgenogram of the abdomen was taken immediately after admission to the hospital. Numerous gaseous distended loops of small and large bowel were seen but fluid levels, localized collections of gas, or a definite point of obstruction was not seen.

It was apparent that the patient had a low incomplete type of intestinal obstruction, chronic in nature and nonstrangulating in character. He was dehydrated and in need of abdominal decompression, but immediate surgical intervention was not indicated. A Miller-Abbott tube was inserted into the stomach and its contents aspirated. After passage of the tube into the duodenum the balloon was inflated and continuous suction siphonage started. The necessary intravenous fluids, a course of sodium sulfadiazine and penicillin, and the usual vitamins, were administered.

The hemoglobin was 70 per cent, the erythrocyte count 3,200,000 per cubic millimeter, and the leucocyte count 9,650 per cubic millimeter of which 75 per cent were polymorphonuclear neutrophilic leucocytes and 25 per cent were lymphocytes. A slight shift to the left with many band forms and toxic granules was noted among the polymorphonuclear neutrophilic leucocytes. Urinalysis revealed only a few clumps of white blood cells and the Kahn reaction was negative. The nonprotein nitrogen of the blood was 40 mg. per cent, the blood chloride 480 mg. per cent, and the carbon dioxide combining power 51 volumes per cent. The roentgenogram of the chest revealed both lung fields to be clear, the domes of the diaphragm to be smooth, and the heart to be of normal size.

The troublesome hiccup disappeared, the nausea and vomiting did not recur, and the patient passed small amounts of liquid stool and flatus on the following day with considerable alleviation of the abdominal distention. A good response to suction siphonage and to warm rectal irrigations was being obtained. The second scout roentgenogram of the abdomen confirmed the clinical impression of progressive decompression. The tip of the Miller-Abbott tube was seen to be in the jejunum. The administration of 500 c.c. of citrated whole blood further contributed to his improvement.

Gradual progressive recovery was manifest during the subsequent period. The patient continued to pass small amounts of flatus through the rectum. A second transfusion of 500 c.c. of citrated whole blood was administered.

Proctoscopic examination at the bedside revealed the mucous membrane of the upper third of the rectum to be grayish white in color and edematous, but ulcerations or a mass were not seen. A barium enema was administered and fluoroscopic and roentgenographic examination disclosed a definite partial obstruction in the sigmoid portion of the colon (Fig. 1), possibly due to inflammatory mass or neoplasm. Numerous small pockets, suggesting diverticula, were present and a small amount of barium was seen to pass into the more proximal portion of the colon. The etiology of the obstructive process was not determined.

It was evident from the time of admission that a colostomy would be necessary to decompress the abdomen effectively. However, the patient was so ill and the evidence for strangulating lesion so completely lacking that immediate or early surgical intervention was contraindicated. Complete relief of abdominal distention had not been obtained, although alleviation had previously resulted. At this time, the distention was becoming more severe. Although the patient was still quite ill, definite improvement in the general condition had occurred. Since a maximum response to nonoperative therapy had been achieved, it was felt that the optimum time for establishment of an operative vent proximal to the obstruction had arrived.

A simple loop colostomy in the right portion of the transverse colon was established. Nothing more was done at this time since expeditious conduct of the procedure was desired. When the closure of the abdominal wall had properly been completed, immediate further decompression was achieved by the insertion of a catheter in the proximal limb of the exteriorized loop.

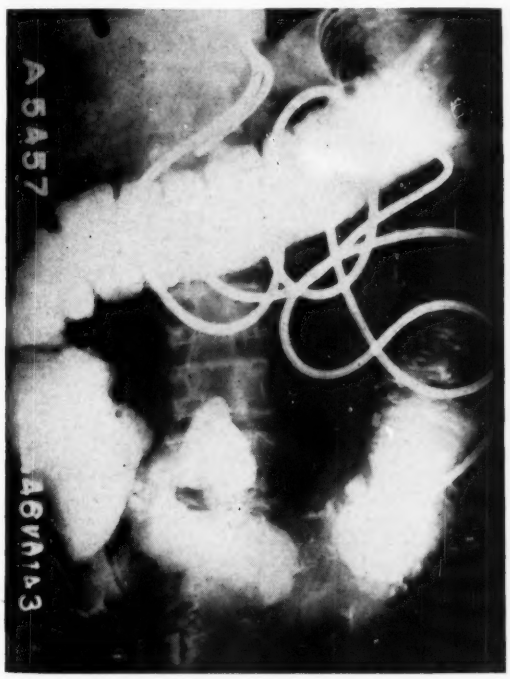

Fig. 1.—Roentgenogram revealing obstructive lesion and the numerous small pockets in the sigmoid portion of the colon.

Postoperatively the course of the patient was somewhat stormy for several days. A bilateral bronchopneumonia was a disturbing complication. However, considerable general improvement was manifest in about one week.

A period of convalescence was strictly in order that the best possible condition of the patient be obtained before surgical attack upon the sigmoid colon. Three weeks after the creation of the colostomy a barium enema was administered again and fluoroscopic and roentgenographic examination of the bowel done. The lesion in the sigmoid colon had not changed during this period. Definite evidence to support a diagnosis of diverticulitis was not found and the usual roentgenographic signs of a malignancy were likewise lacking. It was felt that the patient could have an area of inflammation about several diverticula, a carcinoma, or perhaps both. The suspicion of carcinoma was great enough that plans for exploration and perhaps removal of the offending area of sigmoid were made.

Improvement from this time on was quite rapid. Six weeks after the colostomy had been established, the patient was ready for further surgery.

Laparotomy was performed through an incision in the lower portion of the left rectus abdominis muscle. A firm mass about 6 cm. in length was present in the proximal portion of the sigmoid colon. A considerable number of adhesions were present in the area and the portion of bowel immediately proximal to the lesion was moderately inflammed. Tumors were not palpable in the liver or in the remainder of the gastrointestinal tract. The character of the mass was such that it might be either an area of diverticulitis or a carcinoma, although the diagnosis made at operation was diverticulitis. However, with the realization of the fact that the surgeon is often subject to error during manual and visual examination of any mass, wide extirpation of the involved segment was done. The procedure of choice was extraperitoneal resection with immediate removal of the involved area of bowel. The proximal and distal ends of the mobilized bowel were approximated, the mass was exteriorized, and the affected area of sigmoid removed. Convalescence from this operation was uneventful. About one month later the colostomy in the sigmoid colon was closed and about three weeks following this operation the colostomy in the transverse colon was closed. The patient made a good recovery from both procedures.

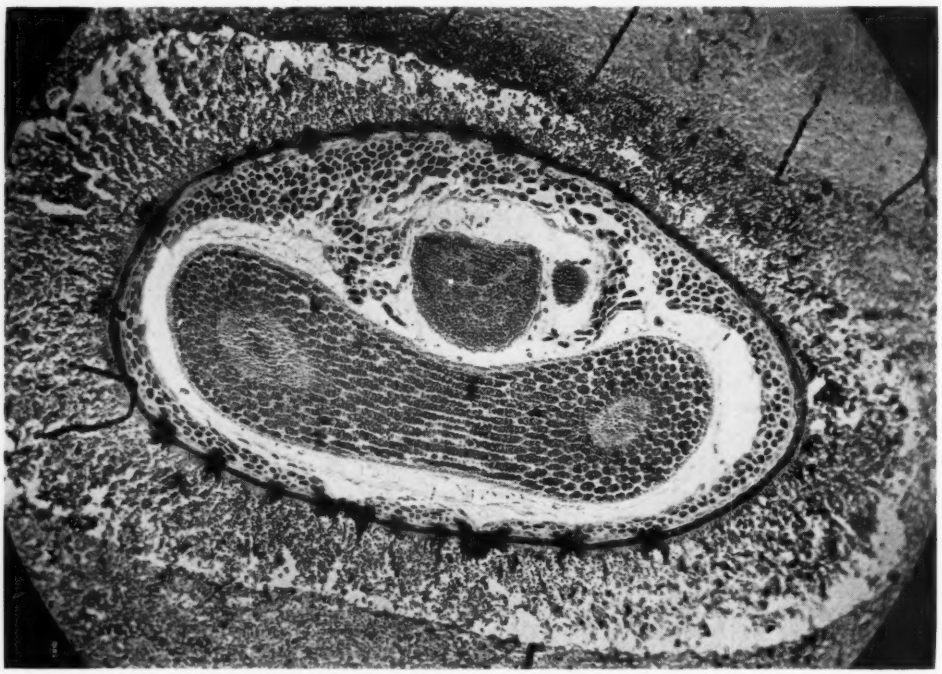

Fig. 2.—An adult female *E. vermicularis* in the wall of the sigmoid portion of the colon.

The pathologic examination* showed grossly the specimen was a segment of colon approximately 15 cm. in length with normal-appearing mucosa but with roughened hemorrhagic serosa at one end. Sections made through the wall of the colon disclosed ten cysts which appeared to lie in the outer part of the muscularis and in the serosa. The cysts varied from 0.4 to 1.0 cm. and were filled with mucus and a small amount of debris which was not frankly fecal in nature. Several of the cysts communicated with the lumen of the bowel through tiny fistulas which contained soft material. The walls of the fistulas were slightly translucent, well defined, and fairly smooth. It was noteworthy that the muscularis in the region of the cysts was not separated in the manner characteristic of diverticula.

*Reported through the courtesy of Dr. William B. VandeGrift.

Miscroscopic examination revealed the mucoid cyst to be entirely serosal in location and surrounded by granulation tissue or a capsule of delicate connective tissue. Numerous plasma cells, polymorphonuclear neutrophilic leucocytes, and polymorphonuclear eosinophilic leucocytes were seen in the granulation tissue. Macrophages surrounded yellowish-brown amorphous hyaline foreign bodies which appeared to be partially phagocytized. A delicate stroma of inflammed granulation tissue was present in the mucoid material. One of the cysts actually was an abscess, and in the purulent material a parasite (Fig. 2) was seen. Yellowish-brown hyaline processes emanated from the surface of the parasite in the manner of a sunburst. The wall of the parasite was formed from externally inward by cuticle, a layer of roughly rectangular cells, and a thin chitinous membrane. A thick layer of muscle lined the inner surface of the wall. Uterus was seen in the center of the parasite but other structures were not found. The fistulous tracts between the serosal cysts and the lumen of the bowel were lined with subacutely inflamed granulation tissue. The mucosa about the orifices of these tracts was chronically inflamed but elsewhere it was normal in appearance. A subacute serosal inflammation opposite the cyst was present. Communication between the cyst and the peritoneal cavity were not found.

The parasitologist* reported that the parasite found was *E. vermicularis*. Morphologically the microscopic section of the parasite possessed typical nematode characteristics such as an outer hyaline, noncellular cuticle, a subcuticular epithelium, and a layer of muscle cells. The particular area of parasite examined was a cross section cut at the greatest width of the body just below the vulva of the adult female worm. The area was approximately 0.5 mm. in diameter and contained part of a distorted uterus which did not hold ova. The distortion and absence of ova may be explicable through the mechanical destruction incident to imbedding and sectioning, through the degeneration caused by long enclosures in the cyst, or through possible natural sterility of the individual adult female nematode.

A number of stool examinations were done but findings in all were negative for parasites, blood, and purulent material. Repeated differential leucocyte counts revealed a normal number of polymorphonuclear eosinophilic leucocytes with the exception of one instance in which they were increased to 8 per cent.

When the final diagnosis was made by the pathologist a course of 1 per cent gentian violet was started. The drug was administered by mouth and also instilled into the distal limb of the colostomy in the transverse colon. A barium enema was given just before the final discharge of the patient from the hospital. Fluoroscopic and roentgenographic examination revealed a slight filling defect at the site of closure in the transverse colon but the bowel was otherwise normal in all respects. The patient was asymptomatic at the time of discharge from the hospital.

The patient returned for examination about three months after the last operation. He stated that he felt quite well, had gained in weight, and did not have any symptoms referable to the large intestine. The abdominal wounds were well healed.

SUMMARY

A case report of a patient who had a chronic type of obstruction of the sigmoid owing to *E. vermicularis* is presented. After intensive preoperative preparation a staged procedure involving resection of the involved area of sigmoid colon was performed. The patient made a complete recovery. The incidence of this particular complication is unusually low in contrast to the reported high human infestation rate with *E. vermicularis*.

*Dr. John Y. C. Watt.

THE RELATION OF PANCREATIC SECRETION TO PEPTIC ULCER FORMATION

Effect of Pancreatectomy, Ligation of Pancreatic Ducts, and Diabetes on the Production of Histamine-Induced Ulcers in the Dog

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A RELATIONSHIP between pancreatic secretion and peptic ulcer formation has been observed for some time. These observations have increased in importance with the advent of vagotomy and its possible modification of the effective parasympathetic innervation of the pancreas and the subsequent influence upon secretory activity. Duodenal ulcers may be produced by the deviation of the alkaline secretion of the pancreas with external fistulas of the type described by Dragstedt, Montgomery, and Ellis[1] and Elman and Hartman,[2] by the internal duodeno-ileal fistula of Mann and Williamson,[3] and by ligation of the pancreatic ducts. These ulcers have usually been considered the result of merely depriving the duodenum of neutralizing influence of the bile and pancreatic secretions on the acid effluent from the stomach. If, however, the duodenum is deprived of the alkaline secretions by pancreatectomy, duodenal ulceration rarely supervenes. The difference may be that whenever the pancreas is present and the external secretions are excluded from the bowel in immediate contact with the gastric secretions ulcers develop, while with simultaneous removal of the internal secretions by pancreatectomy ulcers do not develop when the external secretions are excluded, because the blood sugar remains at a relatively high level without the stimulating influence of hypoglycemia on acid secretion by the glands of the stomach.[4] Dragstedt[5] reported the incidence of experimental peptic ulcers following external pancreatic fistulas as almost 100 per cent (in over 100 cases), following ligation of the ducts as 29 per cent (in 17 cases), and following pancreatectomy as 1.3 per cent (in 300 cases). These figures correspond closely to the observations of other investigators. It may appear that ulcer formation in these situations is not adequately explained by failure of neutralization in the duodenum of the acid effluent of the stomach by the diverted alkaline secretions. Is this paradox real or apparent? Does the pancreas have an intrinsic influence upon ulcer formation other than that of mere alteration of the pH of the duodenal contents?

Certain statistical studies would indicate that peptic ulcer develops infrequently in diabetic patients.[6, 8] In the largest single series Wood[8] reported 94 cases of ulcer in 12,000 diabetic patients, an incidence of 0.78 per cent. Of these however, only 59 were known to have developed ulcers after the onset of

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the diabetes, the remaining 35 having had ulcers when the diabetes was first discovered. The age distribution was unusual in that the onset of 73 of the 94 cases was after the age of 40 years. The symptoms were ordinarily vague with infrequent pain, and hyperacidity was present in only one of the cases of ulcer that developed after the onset of the diabetes. One factor which may be related to the infrequency of ulcer among diabetic patients is the relatively high incidence of anacidity that accompanies diabetes. Anacidity is found in from 20 to 40 per cent of diabetic patients,[9, 10] and the incidence increases with the greater length of duration of the disease.

Both the internal and external secretions of the pancreas may be implicated in ulcer formation. This study concerns certain aspects of the influence of the secretory activity of the pancreas upon the formation of ulcers induced by continuous histamine stimulation of the dog.

METHOD

Sixteen dogs were divided into Groups I, II, III, and IV, of four animals each. Group I served as controls, Group II was subjected to total pancreatectomy, Group III had pancreatic ducts ligated, and Group IV was made diabetic by the administration of alloxan. All of these animals received similar intramuscular injections of histamine-in-beeswax, using the technique of Hay, Varco, Code, and Wangensteen.[12] A large series of dogs which had been pancreatectomized and maintained for long periods on a dietary regime identical to ours was observed by Gregory and his co-workers at this institution and served as controls to demonstrate that ulcers do not develop spontaneously in these animals. Ligation of the pancreatic ducts was performed in three other dogs which were used as additional controls for Group III. When they were sacrificed after 56, 56, and 76 days no ulcers had developed spontaneously. The milk and meat diet appeared to be adequate to protect against ulcer formation. Atrophy of all the pancreas except a thin cord of islet tissue indicated that complete blockage of the ducts was obtained.

Pancreatectomy, Group II.—Total extirpation of the pancreas was performed following in general the procedure outlined by Markowitz.[14] Using aseptic technique under ether anesthesia, an upper abdominal midline incision was made and the duodenum delivered into the wound. The body of the pancreas was closely applied to the concave surface of the duodenum and enveloped the pancreaticoduodenal vessels. Its separation from these structures must be done very carefully, and we found it to be best accomplished by gentle dissection with a moist gauze sponge by actually peeling the pancreas off the duodenum and from around the pancreaticoduodenal vessels. The small pancreatic vessels were merely torn and hemostasis was secured by pressure. The main duct was ligated and sectioned, but the accessory duct did not need to be isolated. The long uncinate process lay free in its mesentery and was readily removed by ligation of its separate blood supply and by dividing the mesentery. The tail was removed in a similar manner, except that it had to be separated carefully from the splenic vessels by gauze and finger dissection. Omentum was wrapped around the duodenum to cover its raw surfaces, and the abdominal wound was closed in layers

with continuous cotton sutures. Postoperatively, careful management and replacement therapy maintained these animals in good condition indefinitely. Twelve hours after operation, milk sweetened with corn syrup was given ad lib, and on the third day ground raw horse meat was added to the diet in increasing amounts. About 15 gm. of lecithin and 4 gm. of pancreatin were mixed with the meat daily. Insulin administration was begun with 3 units of regular insulin twelve hours postoperatively. The dosage was increased with the diet, and it was regulated by frequent blood sugar determinations. Two weeks after operation, when the animal was taking full amounts of meat and milk, the insulin requirements were usually 6 to 8 units of protamine zinc insulin supplemented by 4 to 6 units of regular insulin daily. Fasting blood sugar levels ranging from 217 to 570 mg. per cent indicated the completeness of the pancreatic extirpation. The histamine injections were not started until at least two weeks after the operation. During these injections the dogs received milk ad lib from 8 A.M. till noon and the meat ration at noon. No food was available between noon and 8 A.M.

Ligation of the Pancreatic Ducts, Group III.—Both pancreatic ducts were isolated, cut between cotton ligatures, and the pancreatic stump of the duct was

TABLE I*

GROUP	ANIMAL NO.	WT. IN KG.	DAYS HISTAMINE ADMINISTRATION	BLEEDING	PERFORATION	REMARKS†
I	3	10	44	0	0	Sacrificed, no ulceration present
	4	9	44	0	0	Sacrificed, one small duodenal ulcer (Fig. 1)
	11	6	13	0	0	Sacrificed, one small, superficial duodenal ulcer
	12	5	12	0	0	Sacrificed, one small ulcer at pylorus
II	1	7	7	+	0	Died, numerous ulcers of duodenum and proximal jejunum
	2	12	6	+	2	Died, extensive ulceration of duodenum and jejunum and erosion of mucosa of esophagus (Fig. 2)
	5	14	4	++	0	Sacrificed, multiple duodenal ulcers, 2 esophageal ulcers, extensive gastritis.
	6	11	6	+	1	Sacrificed, 4 duodenal ulcers, hemorrhage, from antrum of stomach
III	7	30‡	2	+	1	Died, extensive ulceration of duodenum and jejunum; one ulcer in stomach 3 cm. in diameter (Fig. 3)
	8	20	4	++	0	Sacrificed, multiple duodenal ulcers; an ulcer in antrum of stomach
	9	10	5	+	1	Died, 4 duodenal ulcers
	10	9	6	+	1	Died, multiple duodenal ulcers
IV	A 8	9	12	0	0	Died, no ulceration present
	A 9	8.5	13	0	1	Died, one large perforated duodenal ulcer
	A10	9.5	15	0	0	Died, no ulceration
	A12	5	10	0	0	Living, no evidence of ulcer

*These four groups of animals received 5 mg. of histamine-in-beeswax intramuscularly per kilogram of body weight daily: Group I, control experiments; Group II, total extirpation of pancreas; Group III, ligation of both pancreatic ducts, and Group IV, rendered diabetic by administration of alloxan.

†Summary of all lesions is given graphically in Fig. 4.

‡This animal received only 100 mg. of histamine-in-beeswax daily.

covered with a mattress suture of cotton through the capsule of the pancreas. The pancreas was completely separated from the duodenum and a bit of omentum was tied in place loosely between the pancreas and the duodenum. The postoperative care and feedings were the same as for the depancreatized animals, except that insulin was not needed.

Alloxan-Diabetic, Group IV.—For the purpose of studying the effect of eliminating the action of insulin, a number of dogs were made diabetic by the administration of 75 mg. of alloxan per kilogram of body weight. The degenerative changes on beta cells by the action of alloxan are not readily accomplished in dogs. By using the technique of withholding food for seventy-two hours as suggested by one of us (L. J. M.), four dogs were made diabetic as indicated in Table I. After stabilizing these animals on daily insulin therapy to maintain reasonable blood sugar levels on the standard milk and meat diet, daily injection of histamine-in-wax was started.

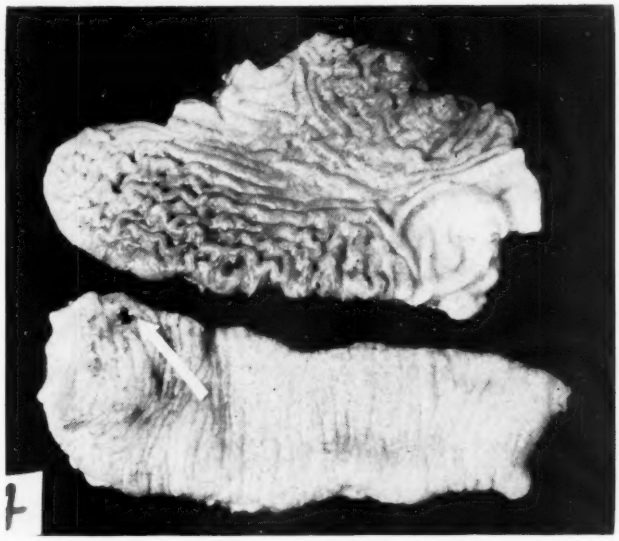

Fig. 1.—Group I, Dog H-4, Control. The animal was maintained on the standard meat and milk diet and received 45 mg. of histamine-in-beeswax intramuscularly daily for forty-four days. The animal was sacrificed and autopsied to show a single duodenal ulcer as indicated. There had been no gross bleeding.

Production of Ulcers.—The histamine-in-beeswax technique was used as described by Hay and associates.[12] The ratio of ingredients used was 1 gm. of histamine phosphate, 0.7 c.c. of beeswax, and 2.9 c.c. of mineral oil, which gives a mixture containing 100 mg. of histamine base per cubic centimeter (1 gm. of histamine phosphate is equivalent to 360 mg. of histamine base). The histamine was ground to a fine powder in a mortar which was kept warm over a water bath. Melted beeswax was added and thoroughly mixed with the powder, then hot mineral oil was added and mixed until a perfectly smooth mixture was obtained. It was then sealed in rubber-stoppered 5 c.c. vials. The mixture solidified on cooling. For injection the vial was heated in a water bath and the mixture was aspirated into a syringe which had been warmed by rinsing it with

hot mineral oil. A 2 c.c. Luer-Lok syringe with a 20 gauge needle was found satisfactory for the injection. The injection was made intramuscularly at a single site into the back muscles. A dosage of 5 mg. of histamine base per kilogram of body weight was administered daily in the late afternoon. The animals were sacrificed when they showed signs of having developed an ulcer. On development of an ulcer the animals refused food, had occasional vomiting and bloody stools, and appeared ill.

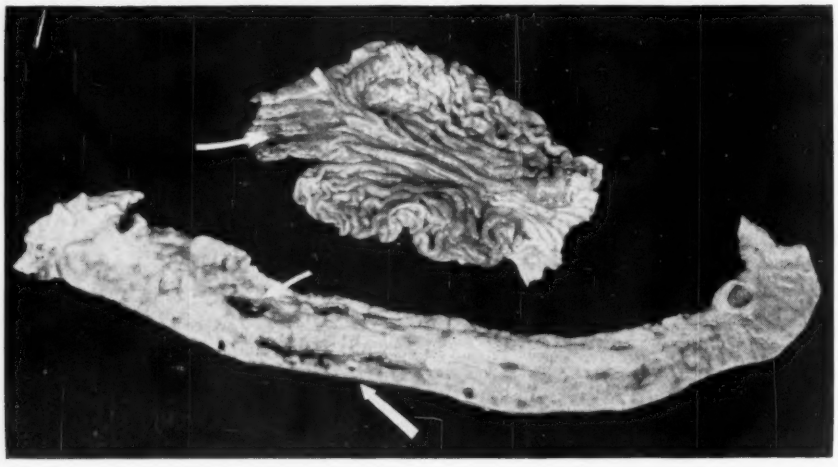

Fig. 2.—Group II, Dog H-2. A total pancreatectomy was done, the animal stabilized on insulin, pancreatin, and a meat and milk diet, and then given 60 mg. (5 mg. per kilogram) of histamine-in-beeswax intramuscularly daily. The animal died on the sixth day and was autopsied to show extensive ulcerations of the duodenum and jejunum and erosion of mucosa of the esophagus. Arrows indicate two perforations in the duodenum.

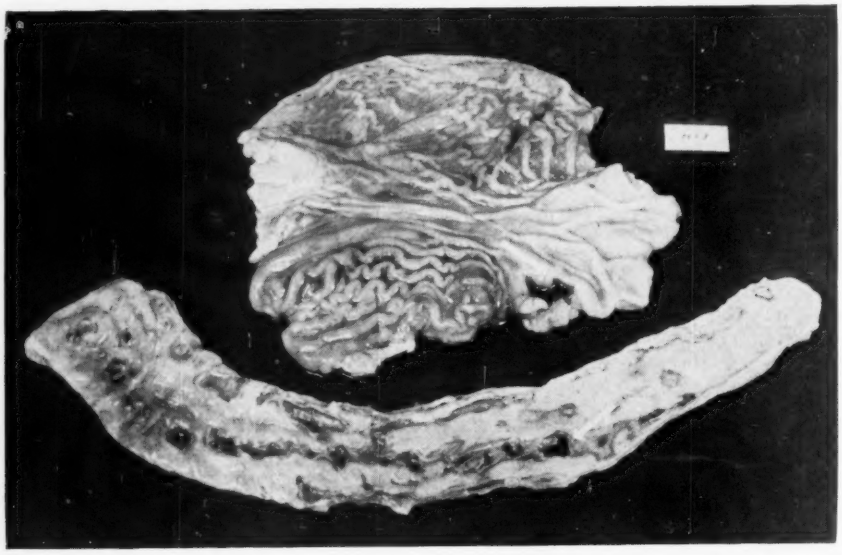

Fig. 3.—Group III, Dog H-7. Pancreatic ducts had been ligated and histamine administered after recovery from operation. This 30 kilogram animal was maintained on milk and meat diet and received 100 mg. of histamine-in-beeswax intramuscularly daily. The animal passed gross blood in stools and died on the second day. Autopsy revealed extensive ulceration of duodenum, jejunum, and stomach with a perforation at junction of duodenum and jejunum.

RESULTS

Control Dogs, Group I.—There were four control animals, two of which were fed a dog biscuit diet, the other two receiving the standardized diet of meat and milk fed to all animals included in this study. The two animals on the routine dog biscuit diet developed typical single ulcers in the first part of the duodenum as shown in Fig. 1. The two dogs that were fed the standard meat and milk diet showed no signs of having developed ulcers. They were sacrificed on the forty-fifth day. One of these dogs had a single small duodenal ulcer; the other had none. Apparently the milk and meat diet prevented the formation of an ulcer in one animal and ameliorated the development of an ulcer in the other. This protection against ulceration further emphasizes the intense reactions observed in the animals of Groups II and III. None of the control dogs had either gross bleeding or perforations.

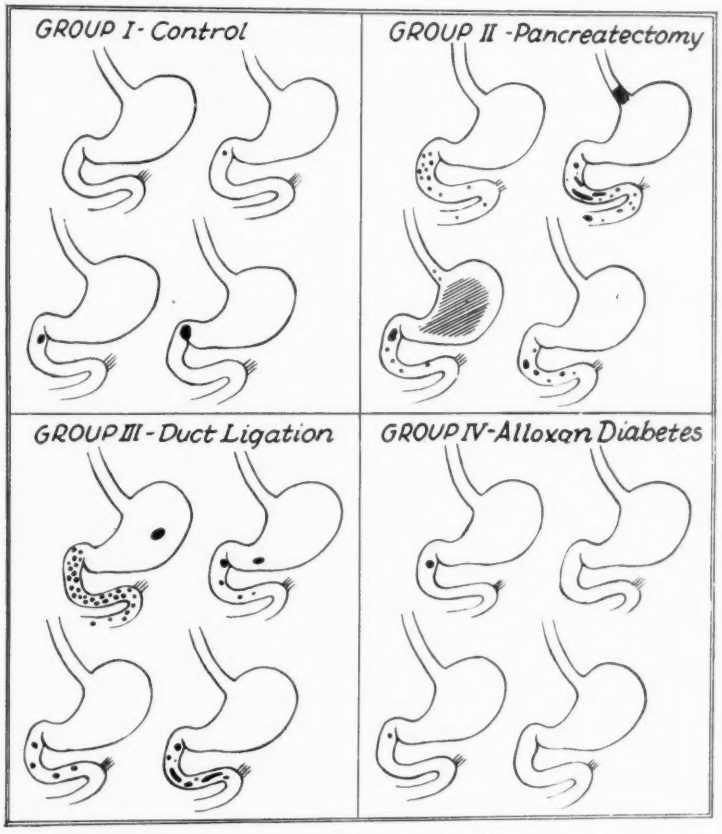

Fig. 4.—Schematic demonstrations of the extent and distribution of ulcerations caused by histamine-in-beeswax with the alterations of pancreatic status.

Depancreatized Dogs, Group II.—The results in the four depancreatized dogs were uniform and striking. Within four to seven days of histamine administration each of the dogs developed multiple severe ulceration of the duodenum. The least severe had four separate ulcers in duodenum, and the most

severe had massive ulceration of the duodenum extending into the jejunum with two separate perforations, as well as erosion of the mucosa of the esophagus (Fig. 2). Of these four animals, two died, two had perforations, and bleeding occurred in all instances.

Dogs With Ligated Pancreatic Ducts, Group III.—The ulcers demonstrated by the group of dogs with ligated pancreatic ducts were even more severe than in the preceding group. One dog died in two days, after only two injections of histamine and showed massive confluent ulceration involving a large area of the duodenum with one large perforation, and also a 3 cm. ulcer in the antrum of the stomach (Fig. 3). Two others died of perforations on the fifth and sixth days, and the fourth was sacrificed after four days. All showed multiple ulcerations, many of them confluent. Gross bleeding occurred in each instance.

Dogs With Alloxan Diabetes, Group IV.—None of the animals with alloxan diabetes showed signs of ulcer formation, although they were all ill probably due to the effect of the alloxan. All of these animals eventually died. A single duodenal ulcer was present in one of the four subjects.

The results observed in this experiment were essentially the same as in the control animals. If the diabetic state in any manner alters the tendency to histamine-induced ulcer formation, the difference is not sufficiently great to permit its demonstration by these studies.

DISCUSSION

Table I gives a summary of the results in each of the four groups. The comparison of the results in the control dogs with those in which the pancreatic secretion has been removed is striking. The two control animals which were placed on the same feeding regime as the dogs operated upon had no symptoms of ulcer and only one of them showed an ulcer after forty-five days. On the other hand, when the pancreatic secretion was diverted from the duodenum multiple severe ulcers developed in from two to seven days. In both the rapidity of development and of extensiveness, the ulcerations were much more severe than have ever been observed in normal animals receiving histamine. It is obvious that the presence of the alkaline pancreatic juice in the duodenum is of great importance in the prevention of ulcers. Although removal of this secretion by extirpation of the gland does not of itself produce ulcers, it is apparent from the results of histamine stimulation that there is a strong predisposition to ulcer formation following pancreatectomy.

That diabetes exerts an inhibitory effect on the formation of peptic ulcers is not borne out by these experiments. The depancreatized animals were completely diabetic, yet they developed ulcers just as rapidly and just as extensively as did the animals that had only the pancreatic ducts ligated. And the alloxan diabetic animals showed no lesser tendency toward induced ulcer formation than did the normal controls.

A point of practical significance that can be derived from these experiments is the fact that removal of the pancreas or ligation of its ducts, as is frequently done in surgical procedures of the duodenum or pancreas, is not without some

danger of postoperative ulceration. It would seem to be advisable to reanastomose the pancreatic duct to the duodenum or jejunum whenever possible following resection of the head of the pancreas. Poth[15] and Cattell[16] have described simple methods of accomplishing this procedure.

It is doubtful that resection of the vagus nerve at the level of the diaphragm should interrupt a sufficient number of the parasympathetic fibers to the pancreas to alter significantly its secretion.

SUMMARY

A series of dogs are injected with histamine-in-beeswax after total pancreatectomy, after ligation of the pancreatic ducts, or after rendering the animals diabetic with alloxan, and the tendency for peptic ulcer formation is observed. It is concluded that the presence of the neutralizing, alkaline secretions per se is of importance in the prevention of ulcer formation and that these secretions should be returned to the proximal portions of the bowel to neutralize the acid effluent of the stomach whenever the normal relationship of pancreatic ducts and duodenum is destroyed.

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THE STOMACH AS A CAUSE OF DIFFICULTY IN INTUBATING THE HUMAN DUODENUM

With Introduction of the Use of the Gastric Balloon

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IT IS not generally recognized that the state of the stomach is an important and avoidable cause of delay or even complete failure in intubating the human duodenum. A study of some 200 cases of small bowel distention since the introduction of the gravity director head in 1944[1] (to be the subject of a later report) has revealed some factors which influence the shape of the stomach, the recognition of which has led to techniques which have materially shortened and facilitated the intubation of the duodenum in both the severest and less severe degrees of distention of the small bowel.

In the early stages of small bowel distention the total volume of the small bowel is not greatly increased. The stomach is able to fill completely, or even to distend if atonic, and to evacuate itself by vomiting, after which its walls will come into apposition. This happens especially where there is retrograde peristalsis of the bowel into the stomach with copious vomiting unrelieved by gastric suction. In other words, there is room in the abdominal cavity for the expansion of the stomach. Under these conditions it is nearly always possible to drop a suitably designed tube, with the aid of gravity, from the fundus of the stomach to the pylorus, especially when the stomach is partially filled with fluid.

Early in the initial series of cases of moderate intestinal distention, in which a thin-walled, flaccid sack of rubber, partially filled with mercury and attached terminally to a tube of adequate lumen was used, it was found possible to intubate twenty successive cases of intestinal distention in an average time of 57.2 minutes, from nose to x-ray evidence of the tube in the duodenum, in the ward and without the aid of fluoroscopy (1945).[2] Continuous gastric suction of the Wangensteen type was not used in any of the cases. No special technique was used other than right-side-lying and rapid advancement of the tube to the length required to reach the duodenum.

Where the stomach has previously been kept empty for some considerable time prior to intestinal intubation, some difficulty may be experienced in bringing the head of the tube rapidly to the pylorus, there to await transference into the duodenum if conditions are favorable. This may even prove impossible with previously described apparatus and techniques where distention has reached a marked degree, with or without continuous gastric suction. Here the distended small bowel is beginning to occupy so large a volume that the stomach is unable to distend unless compensatory mechanisms are taking place. The nature of

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these compensatory mechanisms and their influence on the shape of the stomach is very difficult to evaluate at the present stage of knowledge, owing to the great difficulty of investigating a seriously ill patient. In some cases scientific proof of the facts was obtained from x-ray studies. Only further patient observation will clarify the position so that clinicians will be able to select suitable apparatus in a given set of conditions. It is to be hoped that it will be possible to indicate the type of tube which will be used on a given patient in order to avoid the delay caused by a wrong primary selection. A measurement of the intra-abdominal pressure through the rectum prior to intubation, the assessment of the state of tension of the abdominal wall, the respiratory excursion as indicated by the change of abdominal pressure measured rectally on taking a deep breath, and the height of the diaphragm in x-ray plates are being considered.

The tentative indications which have so far emerged where difficulty may be expected in rapidly transversing the stomach are where the small bowel is distended and the skin of the abdomen is stretched taut, or where the tonus of the abdominal wall, as in a young man of strong muscular build, is maintained in spite of rapid distention of the small intestine. It seems probable that the small bowel only, when distended, influences the shape of the stomach. On the basis of three cases of primary large bowel obstruction with relatively little small bowel distention and in the presence of a greatly distended abdomen in which the skin was stretched taut, no difficulty was experienced in traversing the stomach, although this was anticipated.

Thus, at present it is difficult to indicate a desirable line of approach with a given piece of apparatus except on the basis of trial and error, with the reservations just mentioned. It is hoped that in time this problem may be clarified, either by the development of a universal tube or by a more exact knowledge of the conditions obtaining in the abdomen.

TECHNIQUE

In order to use intubation in cases of moderate small intestinal distention where the stomach has previously been emptied by continuous gastric suction for some time, or where the stomach is pressed upon by the distended bowel for any reason, the technique of air injection into the stomach as suggested by Hamrick (1943),[3] who claimed no originality, has been found to be an extremely useful measure for rapidly traversing the stomach. Instead of using 250 c.c., however, I have found that 400 to 600 c.c. are more successful, since it is usually possible in these cases to get only a few inches of the tube into the fundus of the stomach. It is probable that the use of carbon dioxide, or oxygen, instead of air, will be less likely to add to the distention of the patient. So far, in practice this comparatively small volume of air has not apparently resulted in deterioration of the patient. With this technique it is my practice to pass the tube into the pharynx with the patient lying on his back, after which he is placed upright and positioned well to the left. If his condition permits the legs are hung over the left side of the bed and he leans on a back rest during the swallowing of the tube. This avoids arrest of the tube at the lower end of the esophagus. After the first swallow the tube usually will descend rapidly into the stomach aided by gravity if

well lubricated with a non-oily lubricant. The stomach is then inflated to 600 c.c. and the tube allowed to descend as far as it will go. The patient is then placed in the horizontal right-side-lying position and the intestinal balloon is tested for pyloric contractions. The object of this technique is to avoid arrest of the tube head in the fundus as rarely occurs where the stomach has a shelf known as a Cascade stomach, due, it is thought, to the stomach's flopping over the transverse colon, or due to an elevation in the posterior gastric wall caused by the pancreas. These are the only causes of arrest in the fundus of the stomach which have been discovered so far, apart from the condition of the stomach found in the severest degrees of small bowel distention.

The problem of intubating the severest degrees of distention has occupied the attention of clinicians almost since the introduction to surgery of intestinal intubation by Abbott and Johnston (1938).[4] It is these cases which offer the most anxiety, with the result that the best method of treatment is still in doubt. Surgeons generally dislike operating upon patients with great distention, and if an intestinal tube could be rapidly introduced into the duodenum so that more consistent and earlier decompression in these cases could be achieved, the mortality from uncomplicated bowel distention might be considerably reduced. During a period of one year some ten cases were encountered in which neither air injection with manipulation under fluoroscopy nor waiting for periods of twelve hours for advancement of the tube head into the duodenum has altered the position of the head of the tube. The tendency in these cases has been for the tube to lie just under the diaphragm on the left side. It gradually became apparent, as data accumulated from the use of small quantities of watery barium sulfate, that the fundamental difficulty in intubating these most severe cases of distention is the circumstance that the stomach walls have become pressed together by the distended bowel against the liver to such an extent that air injection will no longer distend the stomach sufficiently to permit passage of the tube (Fig. 1). Distortion, twisting, kinking, and abnormal position of the first and second part of the duodenum have not been found in the limited number of cases (six) in which I have used intubation successfully so far.

There is, moreover, in addition to the problem of accelerating transit of the tube from the stomach into the duodenum, the problem of rather frequent arrest of the tube either in the retroperitoneal duodenum or in the upper reaches of the jejunum beyond the duodenojejunal suspensory ligament. This circumstance is one that interferes seriously with early decompression of the distended intestine. Until this problem is resolved by agents which will permit more consistent early decompression of the distended segments of obstructed intestine, conservative decompression will not have achieved its maximal usefulness. This aspect of the problem is being carefully studied in this laboratory.[2]

Upon recognition of this condition of the stomach in severe cases of distention, a simple method for overcoming the difficulty was devised. The work of Hemmeter (1896)[5] at the Johns Hopkins Hospital suggested that a gastric balloon might be used. Hemmeter was carrying out kymographic studies on the human intestine and he noticed that frequently the balloons were carried

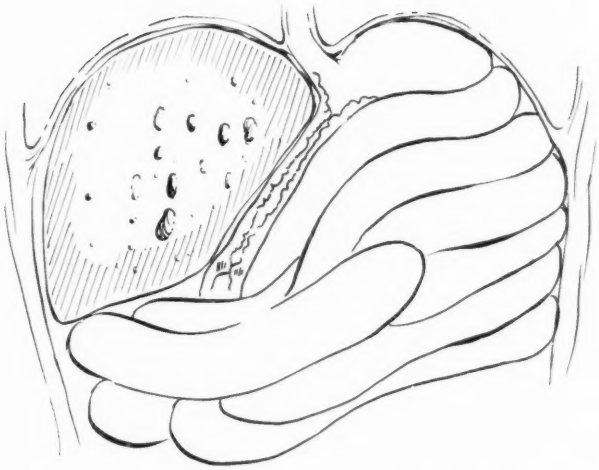

Fig. 1.—Note the distended coils of small bowel and the manner in which a bubble of gas becomes trapped in that part of the fundus of the stomach which lies above the esophageal inlet.

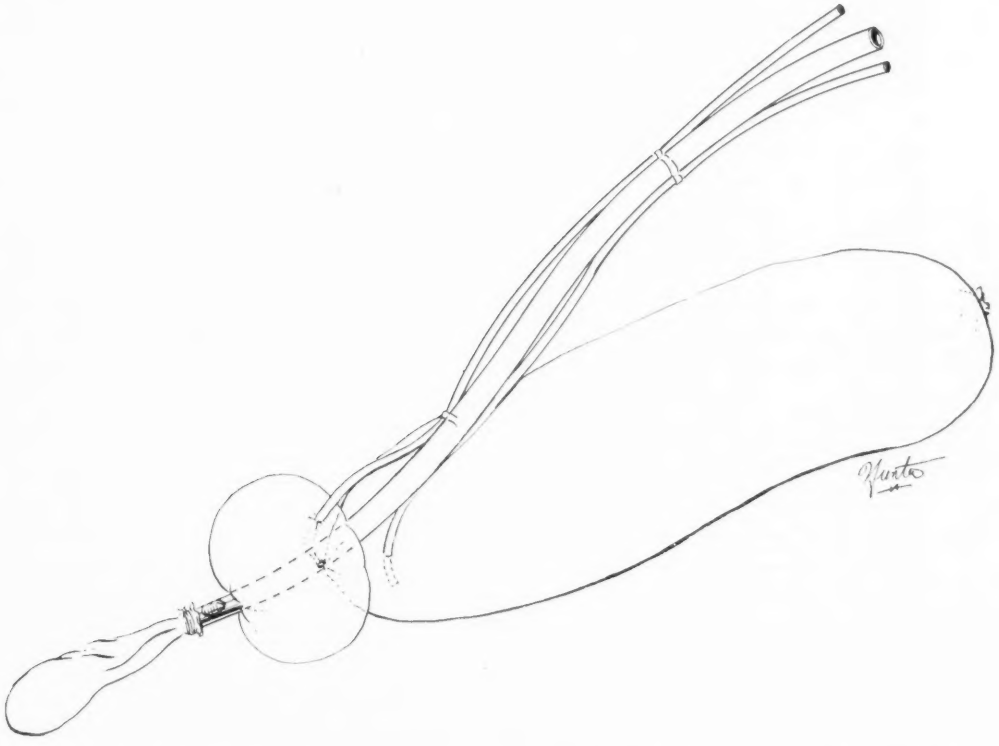

Fig. 2.—The built-up tube is shown. The suction and inflation tubes are of poly-vinyl-chloride resin plasticized with nontoxic and stable plasticizers. The gravity director head contains 40 Gm. of mercury. The aspiration orifice is an oval hole pierced diametrically opposite as near to the end of the tube as possible and just in front of the intestinal balloon so that when the balloon is inflated, the hole is held in the lumen of the gut.

The intestinal balloon is made from a reservoir-ended condom and is tied on in a special way, invaginated on itself so that the air seal is made by rubber-to-rubber bond as the two layers are bound on to the tube which has a full-lumen insert of thin metal just proximal to the aspiration hole.

The gastric balloon is a plain-ended condom tied as closely to the point of attachment of the intestinal balloon as possible. The inflation tube is placed as shown. The open end of the condom is gathered in, stretched, and bound. In this way, owing to the thinner wall toward the open end of the condom, when the balloon is inflated the loose portion inflates first and tends to push the distal portion down the stomach and later occupies the fundus and body of the stomach as maximum inflation is reached. It is extremely important to fix all of the tubes together thoroughly for the first twelve inches, since knotting may occur in use if the gravity director head should double back and fall between any of the tubes. More thorough fixing than that shown should be accomplished. A thin sleeve of latex tube or cement is used.

into the duodenum. He suggested from his observations that it might be possible to construct a balloon with a "magenstrasse" or guiding trough which could be introduced into the normal stomach so that subsequently a tube could be guided down this magenstrasse into the duodenum. It seemed that this scheme would be impractical for this particular application, since after introducing and inflating a balloon in the stomach in severe cases of distention, conditions will be no more favorable for subsequent passage of a tube than before. It was decided to attach the balloon near the distal end of the tube. This was done and an experimental tube was assembled (Fig. 2). It was thought probable that if this balloon were to be partially introduced into the gas bubble which seems always to be trapped in the fundus of the stomach in

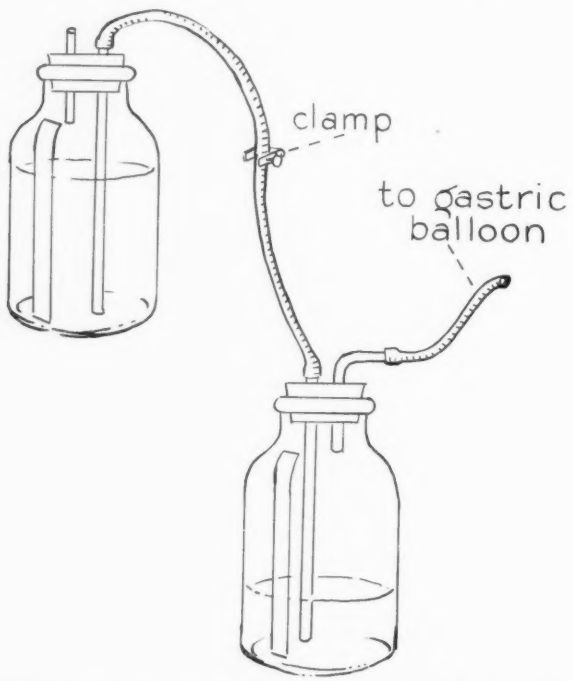

Fig. 3.—The method of inflation in the initial cases in which the gastric balloon was used. The elevated bottle is raised to four feet above the lower bottle.

these cases, and inflated, the walls of the stomach would be forced apart and thus the tip of the tube would be carried to the pylorus. This scheme has been found to work satisfactorily in the limited number of cases so far attempted. In the event that it should be desired to try out this piece of apparatus, I would urge that the details of construction be followed exactly, as many difficulties will thereby be avoided. Further development is in progress. It will be noticed that there are no aspiration holes in the apparatus proximal to the balloon. This is very important, since it may be impossible to get more than the tip of the tube into the fundus of the stomach. Thus, it may be impossible to inflate the fundus somewhat in attempting to get the gastric balloon as far as possible into the stomach. Fluoroscopic visualization has been used regularly on these cases. After getting as much of the gastric balloon and tube into the stomach

as possible without coiling, inflation of the gastric balloon is commenced by displacement of air by syphonage of water from one gallon bottle to another (Fig. 3). The patient should be lying on the right side, feet down, preferably to about 30 degrees or more. As inflation proceeds, more and more of the tube is swallowed with the sipping of water until the patient complains of great discomfort. The air, of course, becomes heated to body temperature and expands, and upon removal more air will seemingly be removed than was put in. The maximum inflation that the patient can stand is used and maintained for only a short time. As much as 1700 c.c. of air have been used. Usually 1500 c.c. are sufficient. Once the head of the tube has been delivered into the pyloric region the gastric balloon is completely deflated and the patient returns to the ward and is placed in the most favorable position for advancement of the tube. Sometimes 5 c.c. of air are put into the intestinal balloon, or into the inflatable gravity director head if this is used in place of the intestinal balloon.

Such, then, is the method, to date, of using the experimental gastric balloon apparatus. Two of the early cases are described here.

CASE REPORTS

CASE 1.—An emaciated white man, aged 40 years, was admitted from another hospital in a highly nervous state with a diagnosis of ulcerative colitis of six months' duration.

Intubation was used in the first instance in order to try to improve his clinical condition prior to operation since he had a low-grade intermittent obstruction. The small intestine at this time was not greatly distended.

Owing to the mental state of the patient it was found necessary to give 4 gr. of sodium amytal over a period of three hours in order to gain his cooperation. Once the tube had been introduced into the nose, the duodenum was intubated in a matter of minutes, as evidenced by a bed radiograph. The patient immediately pulled the tube out and it was replaced into the duodenum at once. Eight hours later the tube was found to be well down the gut and decompression achieved.

The tube was removed in error, and ten days later distention was found to be severe. The skin of the abdomen was stretched taut and the abdominal wall offered considerable resistance to the palpating fingers. A Miller-Abbott tube modified with a gravity director head was inserted, with the help of the patient this time, but it was found impossible to get the tube to advance by pushing into the nostril after it just entered the stomach, as shown by the mark on the tube. A radiograph at this point showed the gravity director head just below the diaphragm and in the fundus of the stomach, lying to the left of the vertebral column. Injection of air into the stomach did not distend the fundus significantly. A tube with a gastric balloon was improvised and inserted into the stomach. After the gastric balloon was inflated, the gravity director head was found to be to the right of the vertebral column in the pylorus (Fig. 4).

At this point the patient became uncooperative and pulled the tube back into the fundus in the night, owing to the omission of the precaution of wrapping his hands. The next morning the gastric balloon was again inflated and the tube delivered to the pylorus. However, by this time it was decided to operate since the possibility of strangulation of the bowel could not be excluded. At operation the bowel was found to have an early impairment of blood supply due to incarceration around the ileostomy. Aseptic decompression[6] with a Wangensteen aseptic decompression set was carried out.

Twenty-four hours afterward, when the patient had recovered from the operation, the intestinal tube which had been left in the stomach was passed into the duodenum by means

Fig. 4 (Case 1).—This shows the gastric balloon inflated to 1500 c.c. of air. The gravity director head with the intestinal balloon is shown carried to the right of the vertebral column. The loops of distended small bowel are seen being forced down by inflation of the stomach.

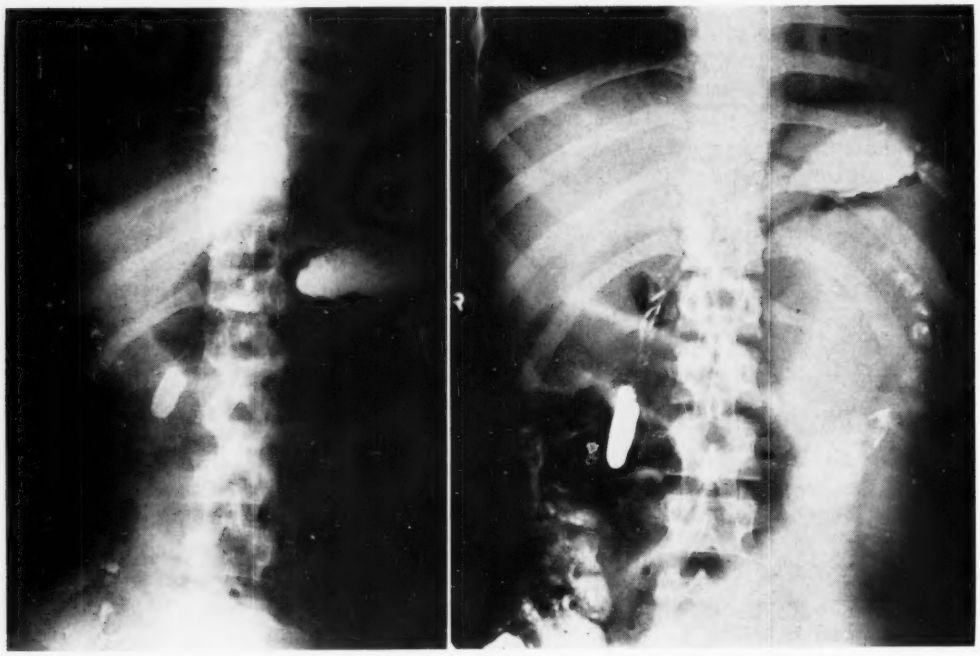

Fig. 5 (Case 2).—This shows the radiograph taken one and one-half hours after introduction of the tube into the nose after manipulation with the gastric balloon.

Fig. 6 (Case 2).—Radiograph taken fifteen hours after introduction of the tube into the nose after the patient remained in a sitting position overnight with the intestinal balloon partially inflated during which time 1400 c.c. of aspirate were obtained. The watery barium sulfate can be seen still in the fundus of the stomach. The walls of the stomach can be seen in apposition. The gravity head is seen in the second part of the duodenum.

The barium in the colon was from a previous barium meal carried out several days before admission and before obstruction became complete.

of the gastric balloon in a matter of minutes. The abdomen following aseptic decompression was now full but not tightly stretched as before. Fifteen hours later the bowel was found to be decompressed and the tube well down the gut.

The following day the patient died. Autopsy revealed multiple lung abscesses.

The points brought out by this case were that a tube could easily be passed into the duodenum of this patient in the absence of distention of the abdomen and that it was possible to get the same tube into the fundus of the stomach in the presence of severe distention; that by using the gastric balloon it was possible to deliver the end of the tube to the pylorus; that after decompression operatively when the abdomen was again soft it was again possible easily and quickly to pass the tube into the duodenum.

This case gave the opportunity to study the gastric balloon, and much valuable time to the patient had to be wasted in discerning what was required. It was unavoidable that the patient had to be taken to surgery owing to prolonged attempts at intubation. It served to show the difficulty of studying these cases scientifically. Nevertheless much valuable information was gained for use in subsequent cases.

CASE 2.—A young white man, aged 16 years, was admitted with a ten-day history of complete obstipation. Five days prior to admission he was given a barium meal since the diagnosis was not clear. The report of this investigation revealed that "the stomach assumed a most peculiar shape due to gas in the small bowel which was not out of shape. The duodenum was slightly dilated, with possibly a partial obstruction of the lower end of the duodenum, not total, as barium passed on into the small bowel."

On admission the abdomen was moderately distended and tense, with good tone of the abdominal musculature. A scar from an appendectomy two years previously was also present. In view of the report of the barium meal and in view of the condition of the abdomen, it was decided to use a gastric balloon. The check radiograph after passage of the tube into the fundus of the stomach showed the gravity director head lying under the diaphragm to the left of the vertebral column. The walls of the body of the stomach were visualized by a faint streak of residual barium lying in apposition transversely at the level of the joint between the tenth and eleventh thoracic vertebrae. A distended loop of jejunum was visualized, below this. Under fluoroscopic visualization 50 c.c. of watery barium sulfate were swallowed. This filled the fundus of the stomach and remained as a composite mass and did not move across to the right of the vertebral column even with manipulation and change of position.

The stomach was then inflated with air by injection down the suction lumen until eructation occurred after every syringeful. This was seen to distend the fundus somewhat but to have no effect on the position of the gravity director head, in spite of various changes of position. The patient was tilted 45 degrees, feet down on the right side, and the gastric balloon inflated to 600 c.c. without distress. The gravity head was seen to move down. More tube was passed and a further advance of the gravity head was observed. There was some doubt as to the position of the gravity head at this stage (Fig. 5), so 50 c.c. of watery barium sulfate were injected down the tube. This barium passed immediately on into the bowel.

Since the patient had vomited the first 50 c.c. of the barium in the meantime, he was given another 50 c.c. of watery barium sulfate in order to visualize the fundus. By this time the time limit of ten minutes had expired and the patient was returned to the ward, one hour and thirty minutes after passage of the tube into the nose. The patient was placed in an upright position overnight with the intestinal balloon partially inflated and with the

gastric balloon completely deflated. During the night 1400 c.c. of drainage occurred and a radiograph (Fig. 6) taken fifteen hours after introduction of the tube showed the tube in the second part of the duodenum, with the barium still in the fundus of the stomach.

The intestinal balloon was inflated fully and the patient allowed to remain on his left side for two hours. A radiograph taken twenty-five hours after introduction of the tube and after 4000 c.c. of intestinal fluid had been removed showed the barium depot in the fundus to have thinned and passed into the gut. The gut was almost decompressed. A further radiograph forty-eight hours after introduction of the tube showed the gut completely decompressed and the end of the tube coiled in the pelvis with an incarcerated mass of small bowel. This was confirmed by fluoroscopic examination with injection of water barium down the suction lumen of the tube after sealing the bowel proximally with the intestinal balloon inflated for a short time to such a degree as to distend the bowel.

The patient was then prepared for operation and put on a liquid diet. Nine days after admission he was operated upon, in good condition, since redistention took place whenever suction was discontinued. No impairment of blood supply of the gut was found and enterolysis was performed and the tube pulled back just proximal to the site of the operation, which was the last four or five feet of the ileum.

On the fourth postoperative day the bowels moved, the tube was removed, and the patient made an uneventful recovery.

SUMMARY

As a result of studying some 200 cases of small bowel distention in which tubes fitted with a thin-walled rubber sack partially filled with mercury and attached terminally were used, the stomach was found to be an important factor in bringing about rapid intubation of the bowel. Techniques for avoiding delay due to the state of the stomach are described, including the use of the gastric balloon developed to force apart the walls of the stomach in cases where gas injection into the stomach will not dilate the stomach sufficiently to permit passage of the tube.

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EXPERIMENTAL STUDIES IN VASCULAR REPAIR

I. Comparison of Reliability of Various Methods of End-to-End Arterial Sutures

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THE technique of vascular repair has assumed increased importance with the advent of vascular shunt operations in such conditions as congenital heart disease associated with reduced pulmonary blood flow[1] and portal hypertension,[2] the introduction of methods of excising and repairing the coarcted aorta,[3, 4] or of by-passing it with a subclavian-aortal anastomosis,[5] and with recent emphasis upon the advantages of maintaining or restoring the continuity of the artery in the surgery of aneurysms and arteriovenous fistulas.[6, 7] Numerous methods of anastomosing and repairing blood vessels have been tried in the past with varying results.[8] Some of these methods have been abandoned while others have continued to be used. In operating for pulmonary stenosis or atresia, Blalock[9] used the continuous everting mattress suture introduced by Clermont[10] and Dorrance,[11] while Potts, Smith, and Gibson[12] employed the continuous over-and-over suture of Carrel.[13] In cases of coarctation of the aorta, Gross[4] used the continuous mattress and Crafoord and Nylin[3] the continuous plain suture. Crafoord[14] also used sutures which do not penetrate the intimal layer, a principle advocated by Jassinowsky.[15] In the repair and anastomosis of peripheral arteries Freeman[6] recently used the Carrel suture, and Shumacker[7] the interrupted everting mattress technique of Jaboulay and Briau.[16]

The literature contains numerous studies which reveal the incidence of successful results and of complications with various techniques in the hands of different investigators; the results obtained with any given method vary considerably. It is apparent that the relative worth of the various techniques can be determined best by controlled experiments performed upon one selected artery in one species of animal by the same group of workers. In this report we wish to present such an effort directed toward inquiring into the comparative reliability of four types of end-to-end repair: interrupted plain, continuous plain, continuous mattress, and interrupted everting mattress sutures.

We have selected these four types of suture for comparison because they represent the cardinal principles of suture methods which have proved most trustworthy. The techniques of plain interrupted through-and-through sutures and of continuous over-and-over sutures embody the accurate end-to-end approximation of the artery wall, the opposed ends of the vessel being maintained in an everted position during the operation by traction sutures. The mattress techniques exemplify those methods which aim at approximation of the artery wall with the intima fixed in an everted position. Continuous and interrupted sutures of both types were selected for study because there are certain theoretical

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advantages and disadvantages of each. Various other methods of repair not included in this investigation are in reality variants of those we have employed.

We have not undertaken to study suture methods which omit penetration of the suture through the intimal layer, such as were originally advocated by Jassinowsky[15] and Burci.[17] They were largely abandoned after the work of Silberberg,[18] Napalkow,[19] and Dörfler.[20] Though Crafoord has used this principle with great success in aortal anastomosis, it is a method which is technically impractical in suturing small arteries and impossible in suturing veins. We have also omitted from consideration nonsuture techniques such as those of Payr,[21] Lespinasse, Fisher, and Eisenstaedt,[22] and Blakemore, Lord, and Stefko.[23] Though such methods undoubtedly have some applicability in certain unusual circumstances and in situations in which vascular repair must be attempted by surgeons untrained in suture techniques, they are not as generally applicable, and have certain disadvantages. In subjecting the suture and nonsuture methods to the critical test of vein-to-vein anastomosis, Johns[24] found the suture method more reliable.

MATERIALS AND METHODS

Mongrel dogs varying in weight from 4 to 44 kilograms were used. Operations were performed under nembutal anesthesia, using aseptic technique. The common carotid arteries were exposed through a transverse anterior incision in the neck. As soon as the vessel was isolated its diameter was carefully measured and recorded. A segment of the artery was then carefully stripped of adventitia.* After applying rubber-shod serrefine clamps proximally and distally, the vessel was cut transversely with small sharp scissors through a little more than half its circumference. The mid-portions of the cut ends were then brought together with the first guide or traction suture. This first suture was placed before the vessel was completely transsected because it saved time and effort in avoiding rotation of one segment of the artery upon the other. The artery was next divided completely and the remaining traction sutures were placed and tied. In the case of small arteries, three of these guide sutures were inserted equidistantly from one another according to the suggestion of Carrel[13]; in the case of larger arteries four were used according to the suggestion of Frouin.[25] All blood was washed from the lumen of the artery with saline solution and the vessel and surrounding tissues were kept moistened throughout the procedure. Deknatel silk, 000000, and round Carrel needles, No. 14, were used; suture and needle were kept lubricated with mineral oil. Care was taken to avoid pinching or otherwise traumatizing the artery.

Traction upon three or four guide sutures triangulated or squared the approximate vessel, opposed the cut ends in a position of eversion, and permitted rotation so as to expose successively the segments of the triangle or square. One segment at a time was sutured. The interrupted plain sutures were simple sutures passed through the entire thickness of the artery from without into the lumen of one segment and then out through the other segment. The continuous

*In this report adventitial stripping is used in the customary surgical sense to indicate the careful removal of the loose, external adventitia. It is obvious that the adventitia is not completely removed.

plain sutures were an over-and-over continuation of such a suture. The interrupted mattress sutures were horizontal "U" sutures; the continuous mattress sutures were a continuation of this same horizontal mattress technique. The continuous sutures were tied to each of the guide sutures, care being taken not to constrict the lumen by drawing the suture too tightly. The interrupted sutures were placed approximately one millimeter apart, the continuous sutures a little closer. The sutures were passed through the vessel wall as near the cut edge as was practical, generally a distance of about twice the diameter of the needle as advised by Deedera.[26] Upon completion of the anastomosis the distal, and then the proximal, clamp was removed and gentle pressure was maintained over the suture line until there was no bleeding. Occasionally it was necessary to use an additional suture in order to achieve hemostasis. The fascia was closed with interrupted silk sutures and the skin with subcuticular or cutaneous sutures of silk. In each animal both carotid arteries were divided and sutured except in occasional animals in which one carotid was excised for histologic or other study. A different method of suture was ordinarily used for each of the two vessels and, in general, the four types of suture were employed in rotation throughout the study. No anticoagulants and no antibiotics or chemotherapeutic agents were used.

Specimens were excised at varying intervals and examined carefully for dehiscence, stricture, thrombosis, aneurysm, and other complications.

RESULTS

Ninety-six sutured arteries were examined at intervals of from four to seventy-six days after operation (average twenty-three days). In Table I data are recorded which give the results with the four different types of suture. It would appear that the mattress techniques gave better results than were obtained with the use of plain sutures, and that interrupted sutures proved somewhat more reliable than continuous sutures. Of twenty-three arteries repaired by the Carrel method, six were thrombosed, in one there was a tiny aneurysm, and in three there were strictures, in one of which a partial dehiscence had occurred. Altogether there were complications in ten, or 43.5 per cent, and in thirteen healing had occurred without complication (56.5 per cent). Of twenty-two arteries repaired with interrupted plain sutures, one was occluded by thrombosis, another was strictured and thrombosed, three others had strictures, one had a small aneurysm, and two had a dehiscence. Complications were present in eight, or 36.4 per cent, while fourteen, or 63.6 per cent, healed without mishap. Of twenty-seven arteries repaired with continuous mattress sutures, four were thrombosed, one was thrombosed and strictured, one had a very small aneurysm, and another had a dehiscence. Complications were present in seven (25.9 per cent), and twenty (74.1 per cent) healed without complications. Of twenty-four arteries anastomosed with interrupted mattress sutures, three were thrombosed, one thrombosed and strictured, and another had a stricture. Altogether there were complications in five, or 20.8 per cent, and no complications in nineteen, or 79.2 per cent. Sixty per cent of the forty-five arteries repaired with plain sutures and 76.5 per cent of the fifty-one repaired with mattress sutures healed without complications.

TABLE I. COMPARISON OF RESULTS OF END-TO-END ARTERIAL SUTURE ACCOMPLISHED BY DIFFERENT TECHNIQUES

TYPE OF SUTURE	PLAIN			MATTRESS			TOTAL
	CONTINUOUS	INTERRUPTED	ALL	CONTINUOUS	INTERRUPTED	ALL	
Number of arteries sutured	23	22	45	27	24	51	96
Number thrombosed	6	2	8	5	4	9	17
Number with stricture	3*	4†	7	1‡	2§	3	10
Number with aneurysm	1	1	2	1	0	1	3
Number with dehiscence	1‖	2	3	1	0	1	4
Number with complications	10 (43.5%)	8 (36.4%)	18 (40%)	7 (25.9%)	5 (20.8%)	12 (23.5%)	30 (31.2%)
Number without complications	13 (56.5%)	14 (63.6%)	27 (60%)	20 (74.1%)	19 (79.2%)	39 (76.5%)	66 (68.8%)

*In one, the lumen was completely closed; in another there was evidence of a partial dehiscence and the lumen was completely occluded; in the third there was a marked stricture but the lumen was patent.

†One of these cases is also listed under thrombosis.

‡Also listed under thrombosis.

§One also listed under thrombosis, the other had a marked stricture without occlusion of the lumen.

‖This case is also listed under stricture.

In analyzing the results of this study it is important to make certain that the outcome in the various groups was dependent upon the type of suture used and not upon some other variable. Except for the difference in the suture technique, most of those factors which might conceivably influence the result were constant. The same artery was used, the same general operative technique, the same operators, and the needles, suture materials, and clamps were identical. Two factors, however, require analysis: the length of time between the arterial repair and the examination of the specimen, and the size of the sutured artery. The first might be of some significance for although such complications as dehiscence and thrombosis undoubtedly occur early, others, such as strictures or aneurysm, might not be evident for some time after the procedure has been accomplished. The second is undoubtedly the most important variable which might influence the result.

In Table II data are listed concerning the interval of time which elapsed between the operative procedure and examination of the specimen. It will be seen that the duration of the anastomoses did not vary greatly in the different groups. The percentage of specimens examined in ten days or less, in from eleven to thirty days, and after thirty days or more was almost precisely the same in the groups repaired by continuous and interrupted plain and continuous mattress sutures. A slightly smaller percentage of those repaired by interrupted

TABLE II. DURATION OF ANASTOMOSES AT TIME OF EXAMINATION

	PLAIN			MATTRESS		
TYPE OF SUTURE	CONTINUOUS	INTERRUPTED	ALL	CONTINUOUS	INTERRUPTED	ALL
Number of arteries sutured	23	22	45	27	24	51
Number examined in 10 days or less	9 (39%)	8 (36%)	17 (38%)	10 (37%)	8 (33%)	18 (35%)
Number examined in from 11 to 30 days	8 (35%)	9 (41%)	17 (38%)	10 (37%)	12 (50%)	22 (43%)
Number examined 30 days or more after operation	6 (26%)	5 (23%)	11 (24%)	7 (26%)	4 (17%)	11 (22%)
Average duration of anastomosis at time of examination, in days	26	23	24	24	19	22

mattress technique were examined in ten days or less and after thirty days or more, and a correspondingly larger percentage in from eleven to thirty days. Of the forty-five arteries repaired with plain sutures, 38 per cent were examined in ten days or less, 38 per cent in from eleven to thirty days, and 24 per cent after thirty days or more. In the case of the fifty-one arteries anastomosed by mattress sutures these percentages were almost the same, 35, 43, and 22 per cent, respectively.

In Table III the data are given concerning the size of the arteries sutured. Very small arteries were used in only 20 per cent of those repaired with plain sutures, and in one-third of those repaired with mattress sutures. Since it is apparent that the chance of success is greater with larger vessels, it is clear that

TABLE III. COMPARISON OF DIAMETERS OF ARTERIES REPAIRED BY DIFFERENT SUTURE METHODS

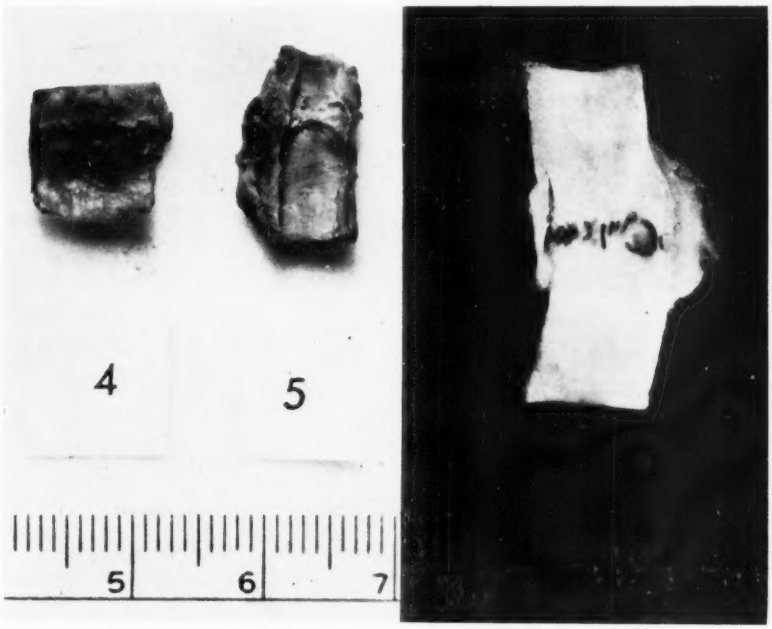
TYPE OF SUTURE	PLAIN			MATTRESS		
	CONTINUOUS	INTERRUPTED	ALL	CONTINUOUS	INTERRUPTED	ALL
Number of arteries sutured	23	22	45	27	24	51
Number with diameter 3.2 mm. or less	5 (22%)	4 (18%)	9 (20%)	9 (33.3%)	8 (33.3%)	17 (33.3%)
Number with diameter of from 3.3 to 4.4 mm.	10 (43%)	10 (45%)	20 (44.4%)	8 (30%)	9 (38%)	17 (33.3%)
Number with diameter of 5 mm. or more	8 (35%)	8 (36%)	16 (35.6%)	10 (37%)	7 (29%)	17 (33.3%)

TABLE IV. COMPARISON OF RESULTS OF END-TO-END ARTERIAL SUTURE ACCORDING TO METHOD OF SUTURE AND SIZE OF ARTERY

TYPE OF SUTURE	PLAIN			MATTRESS		
	CONTINUOUS	INTERRUPTED	ALL	CONTINUOUS	INTERRUPTED	ALL
Diameter of artery more than 3.2 cm.						
Number of arteries sutured	18	18	36	18	16	34
Number thrombosed	3	2†	5	2	2	4
Number with stricture	3*	4†	7	0	0	0
Number with aneurysm	1	1	2	0	0	0
Number with dehiscence	1‡	0	1	0	0	0
Number with complications	7 (37%)	6 (33.3%)	13 (36%)	2 (11%)	2 (12.5%)	4 (11%)
Number without complications	11 (63%)	12 (66.7%)	23 (64%)	16 (89%)	14 (87.5%)	30 (89%)
Diameter of artery 3.2 mm. or less						
Number of arteries sutured	5	4	9	9	8	17
Number thrombosed	3	0	3	3†	2†	5
Number of strictures	0	0	0	1†	2†	3
Number with aneurysm	0	0	0	1	0	1
Number with dehiscence	0	2	2	1	0	1
Number with complications	3 (60%)	2 (50%)	5 (55.6%)	5 (55.6%)	3 (37.5%)	8 (47%)
Number without complications	2 (40%)	2 (50%)	4 (44.4%)	4 (44.4%)	5 (62.5%)	9 (53%)

*One had completely occluded lumen; another had partial dehiscence and complete occlusion of lumen.
†One case had both stricture and thrombosis.
‡Also listed under stricture.

any variation in the size of the vessel favored success in the group in which plain sutures were used. In order to analyze this important matter further the data presented in Table I are broken down in Table IV according to whether the sutured artery was larger or smaller than a diameter of 3.2 mm. It is evident that complications were more frequent when small arteries were sutured, the incidence varying from 37.5 per cent in the case of those repaired by interrupted mattress sutures to 60 per cent in the case of those repaired by the Carrel technique. There were complications in 47 per cent of the small arteries anastomosed with mattress sutures and in 55 per cent of those in which plain sutures were used. The number of small arteries sutured is too small to permit any conclusions concerning the relative merits of the various types of sutures; if anything, the data suggest a trend toward fewer complications with interrupted mattress sutures. Comparison of the results with suture of larger vessels is more informa-



A. *B.*

Fig. 1.—Photographs of arteries repaired by end-to-end suture. *A*, Arteries fifty-eight days after anastomosis by the Carrel technique. Normal (*4*) and strictured (*5*) anastomoses are illustrated. These anastomoses were performed upon femoral arteries and are not included in the series reported; they are typical, however, of similar examples encountered in the present study. *B*, An artery twenty days after end-to-end suture by the Carrel technique. A small aneurysm is present.

tive since adequate numbers of anastomoses were performed. It is seen that the results were considerably better in those arteries repaired with mattress sutures than in those repaired with plain sutures, almost 90 per cent of the former having healed without complications, while only 64 per cent of the latter healed without complication. In the group in which mattress sutures were used, complications were limited to a few instances of thrombosis. In the other group there were examples of stricture, aneurysm, and dehiscence as well.

The gross appearance of a small aneurysm and of a stricture is shown in the photographs in Fig. 1. In Table V pertinent data are recorded concerning

all the complications which occurred. These data simply confirm what is apparent from those already presented. Eight of the seventeen instances of thrombosis (47 per cent) were in arteries 3.2 mm. in diameter or smaller, whereas only 27 per cent of the arteries sutured were of such small diameter. The type of suture apparently was not a great factor in the incidence of thrombosis. With plain suture technique thrombosis took place in five of the thirty-six larger arteries and in three of the nine smaller arteries. With mattress sutures four of the thirty-four larger arteries were thrombosed and five of the seventeen smaller arteries. Three of these seventeen cases of thrombosis were in vessels which also had strictures. Excluding these three cases, six of the seven cases of stricture occurred with plain suture technique and only one with mattress technique. With these included, seven of the ten cases of stricture followed anastomosis with plain sutures. Two of the three instances of aneurysm and three of the four examples of dehiscence similarly occurred with plain suture technique. It would thus

TABLE V. ANALYSIS OF COMPLICATIONS FOLLOWING END-TO-END ANASTOMOSIS OF ARTERIES

COMPLICATIONS	DIAMETER OF ARTERY (IN MM.)	DURATION OF ANASTOMOSES (IN DAYS)	DEGREE	TYPE OF REPAIR	COMMENTS
T	5.2	5	Mild	C.P.	
T	4.0	23	Severe	C.P.	
T	4.0	23	Severe	I.P.	
T	4.5	24	Mild	I.P.	Also stricture
T	4.5	7	Mild	C.P.	
T	5.3	72	Severe	I.M.	
T	3.5	28	Severe	I.M.	
T	5.3	72	Severe	C.M.	
T	4.0	8	Mild	C.M.	
T	3.0	19	Severe	C.P.	
T	3.2	9	Severe	C.P.	
T	2.5	41	Severe	C.P.	
T	3.0	19	Severe	C.M.	
T	3.0	13	Severe	C.M.	Also stricture
T	3.2	17	Severe	C.M.	
T	3.0	13	Mild	I.M.	Also stricture
T	3.2	17	Severe	I.M.	
S	4.5	41	Moderate	I.P.	
S	4.0	59	Severe	I.P.	
S	4.0	70	Severe	I.P.	
S	4.5	24	Mild	I.P.	Also thrombosis
S	4.5	41	Severe	C.P.	Complete occlusion
S	4.0	59	Severe	C.P.	
S	4.3	76	Severe	C.P.	Partial dehiscence
S	3.0	13	Moderate	C.M.	Also thrombosis
S	2.8	38	Severe	I.M.	
S	3.2	17	Moderate	I.M.	Also thrombosis
A	4.2	20	Very small	C.P.	
A	4.2	20	Very small	I.P.	
A	3.0	7	Very small	C.M.	
D	4.3	76	Partial	C.P.	Also stricture
D	2.5	27	Complete	I.P.	
D	2.5	41	Complete	I.P.	
D	3.0	42	Complete	C.M.	

T, Thrombosis.
S, Stricture.
A, Aneurysm.
D, Dehiscence.

C.P., Continuous plain.
I.P., Interrupted plain.
C.M., Continuous mattress.
I.M., Interrupted mattress.

appear that these complications were directly related to the type of suture. Although such complications were nearly twice as common when small arteries were repaired (26.9 per cent as compared with 14.3 per cent), in the group of the larger vessels they occurred in ten of the thirty-six cases repaired with plain sutures (27.7 per cent) and in none of the thirty-four repaired with mattress sutures.

DISCUSSION

There can be no doubt that, regardless of the method of suture used in vascular repair, certain fundamental principles must be followed if the best results are to be obtained. The vessel must be carefully stripped of adventitia so that the adventitia does not fall into the suture line and is not carried into the lumen by the sutures themselves. The vessel must be handled gently and trauma avoided. It must not be allowed to become dry during the procedure. Only fine needles and fine nonirritating nonabsorbable suture materials should be employed. It appears to be of some aid to keep the needle and suture well lubricated with mineral oil or moistened with saline solution. The vessel wall should be approximated with the intimal layer everted. Infection must be avoided.

Our studies would indicate that mattress sutures which fix the opposed ends of the vessel in a position of eversion are superior to plain sutures which bring the ends of the vessels together layer to layer. The superiority of the mattress technique is particularly evident in reference to the avoidance of such complications as dehiscence, aneurysm, and strictures; there was no significant difference in the incidence of thrombosis with plain or mattress sutures. It must be emphasized, however, that thrombosis is the one common complication for which we have a fairly reliable counter measure—the utilization of anticoagulants. We employed no anticoagulants in the present study. Their usefulness in the prevention of thrombosis is suggested by clinical experience and is well established from experimental work. It is of interest that the recent experiments of Kiesewetter and Shumacker[27] reveal that heparin appears to be a better agent than dicumarol in the prevention of intra-arterial thrombosis. Fortunately, anticoagulants can be used safely in operations upon the peripheral arteries.[28] They cannot be used with safety in operations within the thorax or peritoneal cavity. Fortunately, too, most of the vascular repairs within these cavities are either upon large vessels such as the aorta where the chance of thrombosis is not great, or are performed to produce a shunt from a high pressure to a low pressure area, where the rapid flow of blood also reduces the hazard of clotting. They can be used where they are most needed, in the surgery of the peripheral vessels. It is significant that Gross and Hufnagel[29] found the continuous mattress suture superior to the continuous plain suture in experimental anastomosis of the aorta, bleeding from the suture line being rare with the former, and common and troublesome with the latter method. We also noted less bleeding when mattress sutures were used. It would seem plausible that bleeding at the time the anastomosis is completed may increase the likelihood of subsequent complications.

Our studies demonstrate a fact which has appeared evident from other experimental and clinical work, namely, that the chance of success in arterial suture is definitely reduced when one is working with a vessel of extremely small

size. Too few anastomoses were performed upon such small arteries to yield significant data concerning the relative merits of the various suture techniques.

Although the experiments demonstrated a significant advantage of the mattress over the plain sutures, there was no convincing evidence that the interrupted sutures were superior to the continuous sutures or vice versa. In actual practice there also seems to be little advantage of one method over the other. Theoretically, continuous sutures have the disadvantage that they may be drawn too tightly and thus may produce some constriction. Should a continuous suture break it would obviously subject the anastomosis to greater chance of disruption. Continuous sutures, on the other hand, are placed with a little more ease and rapidity. In patients, it has been the practice of one of us (H.B.S.,Jr.) to use interrupted mattress sutures where the vessels are easily accessible, as in the case of the peripheral arteries, and continuous mattress sutures in procedures where approximation is more difficult and where there is poor access to certain portions of the suture line once the anastomosis is completed, as in the Blalock operation and in coaretation of the aorta.

It should be pointed out that the neck was not splinted in any of our animals. It is entirely likely that proper splinting to avoid any strain upon the suture line might have influenced the results favorably. In other experiments[30] we have found that the recently sutured vessel will withstand, without leaking or bursting, intraluminal pressures far in excess of the systolic blood pressure even in hypertensive states. They can, however, be pulled apart by a relatively small force directly applied.

It must be emphasized that normal arteries were used in these experiments and that the anastomoses were performed by operators who had fairly extensive experience with methods of vascular repair. It is not unlikely that the advantage of the mattress technique which was evident in our experiments might be amplified in arterial surgery upon somewhat damaged or diseased arteries in man, or in the hands of operators with relatively small experience in vascular suture techniques.

SUMMARY AND CONCLUSIONS

The experiments reported demonstrate that end-to-end arterial repair is attended by a fairly high incidence of complications when very small arteries are used, irrespective of the type of suture. With arteries of moderate size the incidence of thrombosis does not vary greatly with different methods of repair, but other complications such as dehiscence, stricture, and aneurysm are much less frequent when everting mattress sutures are used. It is believed that mattress techniques will prove most reliable in man. Judicious use of anticoagulants, of antibiotics or chemotherapeutic agents when indicated, and of proper splinting when necessary to avoid tension will likely add safety to the repair and anastomosis of arteries.

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THE TREATMENT OF EXPERIMENTAL UREMIA BY INTESTINAL LAVAGE

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RECENTLY, several investigators have attempted to develop a practical means of removing retention products in cases of acute renal failure. The search for such a means is predicated on the theory that given time, the kidneys may be able to recover function that has been temporarily damaged by such means as transfusion reactions, sulfonamide toxicity, the crush syndrome, toxemia of pregnancy, mercury poisoning, and surgical trauma to the urinary tract.

Three main methods for the removal of retention products have been investigated: (1) peritoneal lavage,[4, 17-23] (2) dialysis of the blood outside the body and returning it to the circulation,[5-7] and (3) intestinal lavage.[2, 8, 9, 16] The first two methods have received more attention than has intestinal lavage and already have been given a clinical trial with varying degrees of success. The clinical use of intestinal lavage has been very limited and has received relatively little attention. Except for the work of Kolff and Bliss, the experimental side has been neglected.

This communication deals with the experimental results obtained from the lavage of isolated intestinal loops in dogs rendered uremic by means of bilateral nephrectomy. This problem was suggested to one of us (H.N.H.) by the late Dr. Edmund Andrews in 1934 and a few very preliminary experiments were carried out at that time.

METHODS

Preparation of the Animals.—The animals used in these experiments were healthy mongrel dogs weighing from 5.5 to 17 kilograms. Under nembutal anesthesia, intestinal segments with attached mesentery and blood supply were isolated and each end of the segments was sutured to the abdominal wall and skin so as to form a Thiry-Vella fistula.[10] Continuity of the intestine was restored by an end-to-end anastomosis. The length of these segments varied from 20 to 40 inches. In the animals included in this series, the proximal end was approximately 5 inches below the ligament of Treitz. Eleven to twenty-eight days later, when the incisions had thoroughly healed, a bilateral nephrectomy was done under ether anesthesia through bilateral paravertebral incisions.

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The animals were kept on a routine kennel diet and water ad lib. throughout the entire experiment except during the periods of irrigation. No medications except intravenous calcium gluconate were given.

Method of Irrigation.—A Foley type catheter was placed in each end of the intestinal segment. The wash fluid was allowed to drip into the proximal end from an overhead reservoir and collected from the distal end in a carboy. During the irrigation periods the dogs were placed on an animal table and maintained in position by means of loose restraining bands. The rate of flow of the wash fluid was from 26 to 66 c.c. per minute. Four different fluids were used: (1) normal NaCl; (2) 3 per cent NaCl; (3) NaCl 6.1 Gm., $CaCl_2$ 0.23 Gm., $CaHPO_4$ 0.07 Gm., and Na_2So_4 10 Gm. per liter of solution; and (4) NaCl 6.1 Gm., $CaCl_2$ 0.23 Gm., KCl 0.35 Gm., $NaHCO_3$ 2.2 Gm., Na_2SO_4 30 Gm., and glucose 10 Gm. per liter of solution.

Irrigation was intermittent and was begun 21 to 50 hours after nephrectomy. Single irrigation periods lasted from 2.5 to 10.5 hours. No animal was irrigated more than 10.5 hours in any one 24 hour period.

Chemistry.—In the control animals, blood urea nitrogen and nonprotein nitrogen determinations were made twice a day. In the irrigated animals the blood urea nitrogen, nonprotein nitrogen, and hematocrit values were determined at the beginning and end of each irrigation period. Urea nitrogen and nonprotein nitrogen values were determined on each sample of wash fluid. Duplicate determinations were made as a check in each case. Heparin was used as the anticoagulant for all blood samples. Urea and nonprotein nitrogen determinations were done by a modified Gentzkow[11] method. The Van Allen hematocrit tube was used in determining the hematocrit values. Since the urea and nonprotein nitrogen values paralleled one another closely only the urea nitrogen values will be presented here.

RESULTS

As was to be expected, both the control and the irrigated dogs showed a considerable weight loss between the formation of the Thiry-Vella fistula and the nephrectomy. Actual weight loss varied from 1.2 to 7.8 kilograms and the percentage weight loss varied from 11 to 45 per cent. The irrigated animals lost on an average 8 per cent more weight than the controls. No correlation could be found between the weight loss and the survival time. However, the three irrigated dogs which averaged the longest survival time also averaged the greatest loss in weight (37 per cent).

There were five control dogs used in these experiments. The survival time after nephrectomy ranged from 52 to 104 hours with an average of 73 hours. The terminal blood urea nitrogen levels varied from 145 to 265 mg. per cent with an average of 193 mg. per cent. The average rate of rise of the urea nitrogen was 2.5 mg. per cent per hour.

Uremic symptoms appeared in most of the control animals at 36 to 48 hours after nephrectomy and were clearly manifested at about 60 hours. Actual coma did not supervene until shortly before death. At autopsy none of the animals

showed gross edema and only one appeared to be slightly dehydrated. The length of the loops in the control group had no effect on the survival time.

The data on the irrigation experiments are shown in Table I. A graphic representation of the results obtained in one dog (No. 44) is shown in Fig. 1. Eighteen irrigation experiments were carried out in six dogs. The results in three other dogs are excluded, since at autopsy two of these had bilateral bronchopneumonia and the other had a large abscess in each nephrectomy incision. Two of the discarded animals had low ileal loops in which the distal end was 5 inches proximal to the ileocecal valve. No appreciable difference in the amount of urea removed by lavage could be attributed to the site of the loop.[2] In those six irrigated dogs used as the basis for this report, the average survival time was 81 hours, only 8 hours longer than that of the controls. The survival times ranged from 63 to 99 hours. The terminal blood urea nitrogen levels ranged from 89 to 229 mg. per cent, with an average of 144 mg. per cent. This is 49 mg. per cent lower than the average terminal urea nitrogen level in

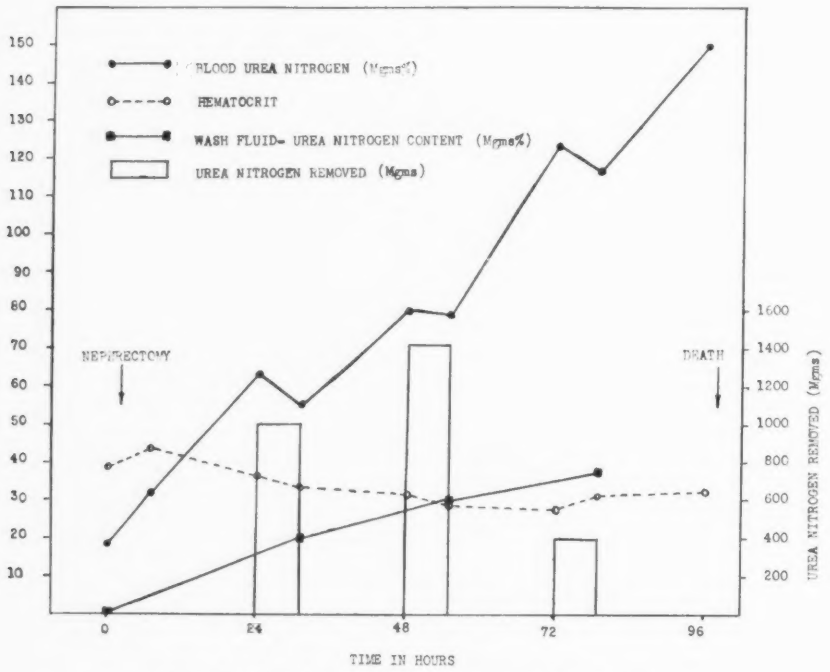

Fig. 1.—Results of intestinal lavage in Dog 44.

the controls. The average rate of rise of the urea nitrogen was 1.6 mg. per cent per hour during the entire survival period, including both the irrigation and the nonirrigation periods. The blood urea nitrogen was kept level or was lowered 1 to 9 mg. per cent during the actual irrigation period in 8, or 44.5 per cent, of the experiments. In 10, or 55.5 per cent, the urea nitrogen rose 1 to 25 mg. per cent. The maximum efficiency in urea removal was in Dog 32 where 14 mg. of urea nitrogen were removed per inch of intestine per hour of irrigation. The poorest result was obtained in Dog 48 where the wash fluid was

TABLE I. RESULTS OBTAINED IN INTESTINAL LAVAGE

DOG NO.	LOOP LENGTH (IN.)	SURVIVAL TIME (HR.)	HR. WASHED	BLOOD UREA NITROGEN (MG.)		HEMATOCRIT		UREA NITROGEN REMOVED (MG.)		FLUID USED	UREA NITROGEN IN WASH FLUID (MG. %)
				INITIAL	TERMINAL	INITIAL	TERMINAL	TOTAL	PER IN. PER HR.		
24	34	63.5	4	141	142	60	55	408	3	1	3.8
			2	142	150	55	53	615	9	2	7.7
25	30	63	2.5	53	53	40	40	323	3.4	1	6.4
			3	53	53	40	40	256	3.6	1	3.3
			2.3	53	61	40	40	240	3.6	1	2.7
			6	70	94	33	29	862	4.8	1	4.9
			4	94	93	29	33	374	3.1	1	2.9
28	37	72	7	49	53	41	39	921	3.5	3	4.9
			10.5	62	59	36	38	1417	3.6	3	4.4
32	20	98.5	7	114	124	44	43	1435	10.3	4	9
			6	166	161	46	44	1440	14	4	8
			3.5	204	229	43	43	622	8.9	4	7
44	38	96	7	64	55	37	34	1000	3.8	3 (Reused)	20
			7	80	79	32	29	1450	5.5	3 (Reused)	29
			7	124	117	28	31	400	1.5	3 (Reused)	37
48	35	95	7	48	54	25	25	900	3.6	3 (Reused)	18
			6.5	83	86	23	23	800	3.5	3 (Reused)	34
			5.5	113	118	22	20	250	1.3	3 (Reused)	39

reused and during one period only 1.3 mg. were removed per inch per hour. At the time when this low return occurred, the wash fluid contained between 34 and 39 mg. per cent of urea nitrogen. A similar low value occurred in Dog 44 when there was 29 to 37 mg. per cent of urea nitrogen in the reused wash fluid.

Best results were obtained with hypertonic fluids when 3 per cent saline solution was used alone or when 3 per cent sodium sulfate was added to the wash fluid and relatively more urea nitrogen was then removed. Apparently some urea is excreted actively into the lumen of the bowel during the resting phase,[12] since when the bowel is washed clean of urea with water, a small amount can be obtained from the lumen several hours later (Table II). It is felt that the hypertonic solutions accelerate the excretion by producing a chemical or physical irritation of the mucosa[13] rather than by a purely osmotic process. This excretion does not appear to be perceptibly accelerated by a high blood urea level, but rather is a constant slow process.

As can be seen in Dogs 44 and 48 (Table I), a high urea content in the wash fluid diminishes the amount of urea removed from the blood stream. This

TABLE II. EXCRETION OF UREA BY THE RESTING SMALL BOWEL

DOG NO.	LOOP LENGTH (IN.)	BLOOD UREA NITROGEN (MG.%)	TIME SINCE LAST WASHING (HR.)	UREA NITROGEN EXCRETED INTO LOOP (MG.)
28	37	12.5	17	7
27	38	12	24	10
25	30	11.5	24	7
24	34	10	24	12
18	37	14	24	10
16	34	18	48	30
3	25	173	52	10
16	34	160	75	30
18	37	221	81	20
9	23	265	104	20

was also evident in several other dogs which are not included in this communication.

In only three of the washing experiments did the hematocrit rise during the actual irrigation period. In the remainder, the hematocrit stayed level or dropped one to five points. Hence, even though the wash fluid was hypertonic, these animals were able to extract water from it. From 50 to 250 c.c. less fluid were recovered than was originally used.

Extensive chemical analyses were not performed so we were unable to follow the fluid and electrolyte pattern. It was very obvious that this was markedly disturbed. Some of the animals that appeared to be in good condition at the beginning of the irrigation period later showed marked muscular incoordination and irritability, tremors, convulsions, and vomiting. After the irrigation was completed, they were unable to stand or walk and appeared completely disoriented. This condition occurred even when the blood urea nitrogen remained level or was lowered. Moderate recovery occurred in the overnight rest periods between irrigations. Large doses of calcium gluconate intravenously gave only partial relief. In those cases where the wash fluid was reused throughout the survival time, this symptom complex was much less apparent. This picture seems to resemble somewhat that seen in animals fed sea water.[14, 15] Further studies are under way to determine the cause of these symptoms and to obtain a comprehensive picture of the electrolyte pattern.

DISCUSSION

The results obtained with intestinal lavage by various workers have been conflicting. Seligman and associates[2] estimated that ten feet of bowel as an isolated segment would be required to supply 10 per cent of the maximum normal renal clearance (75 ml. per minute). In one uremic patient they were able to extract not more than 1 Gm. of urea in a 24 hour period by gastroduodenal suction. In this same patient, irrigation of 10 inch isolated loop of ileum removed only 0.1 Gm. of urea in 24 hours. Bliss and co-workers[12] found gastroduodenal irrigation in uremic dogs disappointing.

On the other hand, Goudsmit[5] was able to remove 10 Gm. of urea in 7¾ hours by forced intestinal irrigation with hypertonic sodium sulfate solution. He stated that there were no significant changes in the blood urea level. Ochsner[9] mentioned two cases of renal shutdown following incompatible blood reactions in which gastric lavage was instituted. In both cases the nonprotein nitrogen in the blood was lowered and maintained at a low level for 10 and 14 days, respectively. Both patients recovered. Kolff[16] was able to remove as much as 5 Gm. of urea in 10 hours by perfusion of an ileal loop one meter long.

We believe from our small number of experiments that intestinal lavage can produce a lowering of the blood urea nitrogen in a significant number of cases and that fairly large amounts of urea can be removed. Taking the results of one of the experiments in Dog 28 and all of them in Dog 32 as representative (hypertonic fluid was used in these experiments), one could expect to remove 252 mg. of urea nitrogen per 24 hours per inch of intestine irrigated.

In a 36 inch segment this would amount to about 19 Gm. of urea in 24 hours. While this is less than can be obtained by peritoneal lavage it is a significant amount.

The exact nature and cause of the "irrigation syndrome" encountered in these animals are not entirely clear. This syndrome is probably based on an electrolyte upset. That hypocalcemia plays a part is evident from the slight improvement following intravenous calcium. It seems logical to assume that the electrolyte upset itself is at least partially due to the selective absorption of the intestine, since this organ by no means acts as a simple semipermeable membrane. Hence, a fluid which is ideal for peritoneal lavage could not be expected to perform as well in intestinal lavage. The main difficulty to be overcome consists in finding a wash fluid which will not distort the electrolyte and fluid balance and at the same time will allow maximum diffusion or excretion of urea into the bowel. On the basis of these experiments it is difficult to prognosticate what the final composition of that fluid will be. It is probably safe to state that hypertonicity due to a poorly absorbed substance such as sodium or magnesium sulfate should be present to aid in the removal of greater amounts of urea and to prevent edema.

Clinically, of course, it would not be feasible surgically to isolate small bowel loops. If, with further investigation, the procedure shows greater promise, irrigation could be carried out with a modified Miller-Abbott tube as was used by Goudsmit.[8]

SUMMARY

1. The results of experiments with intestinal lavage in experimental uremia are presented.

2. The prolongation of life in the irrigated animals as compared to the control animals is not significant, probably because of a severe upset in the electrolyte pattern.

3. Fairly large amounts of urea can be removed by intestinal lavage, but the problem of electrolyte balance remains to be solved.

4. The possibility of more widespread clinical application is mentioned.

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THE NEUTRALIZATION OF HEPARIN BY PROTAMINE

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THERE has been little interest in an antidote for heparin, probably because the simple expedient of stopping its administration is followed by a restoration of the normal clotting time of the blood in an hour or two. Nevertheless, it is easy to imagine situations where it would be desirable to correct a hemorrhagic tendency in a matter of minutes rather than hours. In 1937, Chargoff and Olson[1] reported that the activity of heparin could be entirely stopped by the intravenous injection of a protamine (salmine, from salmon spermatozoa). They were investigating the anticoagulant properties of heparin and attempted to prolong its transient action by combining it with another substance. They reasoned that if protamine delayed the absorption of insulin, it might do the same for heparin. However, they found that the effect of heparin was nullified by the protamine. Apparently, the two substances form a stable salt which has a low degree of dissociation.

The experimental work on dogs was applied to human beings by Jorpes, Edman, and Thaning.[2] They neutralized the effect of heparin in ten individuals by giving the protamine clupeine (from the herring) in the amount of 60 mg. for each 100 mg. of heparin.

The American literature contains no record of protamine being employed to counteract the action of heparin. Instead, there are two statements which would discourage its use. In a review of the subject of heparin, Mason[3] said, "Protamine is toxic if administered in any form intravenously." The same statement occurred in a recent review of the literature on the management of arterial embolism.[4] Therefore, it seemed desirable to repeat a part of the work of the other investigators. We were particularly interested to see if nontoxic protamine is easily available in this country.

Two preparations of protamine were used in the experiments.* We were supplied with some ampules of the solution used by the Swedish group.* This consisted of a per cent solution of protamine sulfate (clupeine). Presumably, this was prepared according to the method described by Jorpes.[5] "The pure protamine sulfate from herring or salmon is dissolved in dilute hydrochloric acid, pH 3, and sterilized in an autoclave. It produces no undesirable reactions." The material used in most of the experiments was prepared by dissolving protamine sulfate (salmine†) to make a 2 per cent solution. Sterilization was obtained by passing it through a Berkfeld filter, and phenol (to make 0.5 per cent) was added as a preservative.

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†Furnished by Eli Lilly and Company, Indianapolis, Ind.

Experiments were carried out on six dogs varying in weight from 10 to 30 kilograms. A sample of blood was withdrawn for the determination of the normal clotting time, after which heparin (1 mg. per kilogram) was injected through the same needle. The clotting time was determined by the Lee and White method (inversion of test tubes). Twenty minutes after the injection of heparin a second sample of blood was withdrawn and protamine sulfate, 1 mg. per kilogram, was injected through the same needle. Six to ten minutes after this injection, the third clotting time was obtained. On a subsequent day, the animals were given identical injections of heparin and their clotting times were taken at thirty-minute intervals to determine the duration of the normal heparin effect.

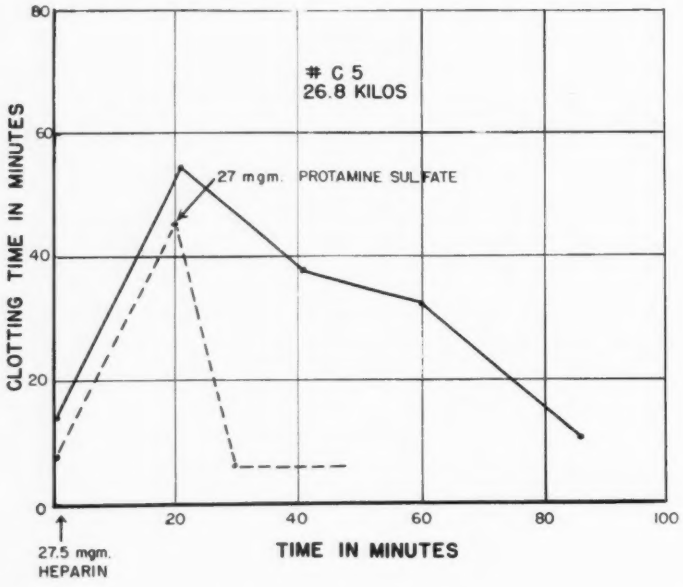

Fig. 1.—Results of a typical experiment on a dog. Solid line indicates the effect of heparin alone. The broken line represents an experiment on a different day, showing the neutralization of heparin by protamine.

Similar results were obtained in each of the six experiments. The heparin injection caused a marked increase in the clotting time, an effect which was immediately abolished by the protamine. The findings in a typical experiment are shown in Fig. 1.

To investigate toxicity, we injected a massive dose of protamine (200 mg. for a dog weighing 20 kilograms). The animal became very excited and confused, but recovered from this reaction in about one minute and subsequently showed no deviation from the normal. The clotting time remained near its normal level (eleven minutes) for one-half hour and then dropped to six minutes. Smaller doses (1 mg. per kilogram) did not change the clotting time in normal dogs.

Since no adverse symptoms were observed in the animal experiments, we extended the tests to man. The results obtained in five individuals are shown in Table I. It will be noted that in every instance the markedly elevated clotting time was brought to normal by the protamine injection.

TABLE I. REDUCTION OF CLOTTING TIME BY PROTAMINE IN FIVE HEPARINIZED PATIENTS (CLOTTING TIME IN MINUTES)

CASE	WEIGHT (KG.)	NORMAL CLOTTING TIME	MG. HEPARIN	CLOTTING TIME 20 MIN. LATER	MG. PROTAMINE	CLOTTING TIME 8 MIN. LATER
1	53	16	50	120	50	15
2	54	15	54	120	54	20
3	80	12	80	90	80	8
4	66	19	80	120	66	17
5	50	12	50	72	50	15

CONCLUSIONS

We have corroborated the findings of previous investigators that protamine sulfate can be used to neutralize the anticoagulant effect of heparin. A nontoxic solution for intravenous use can be easily prepared.

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PATELLA FRACTURES

A Method of Wiring

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BECAUSE of the fact that the incidence of fractured patella is rather common and usually there is a long and complicated convalescence, this study was instigated to seek a better method for treatment of fractured patella in which there is a definite separation of the fragments.

During the five years from June, 1942, to June, 1947, we treated 247 fresh fractured patellae in addition to 22 old referred cases primarily from overseas, Army hospitals, and ship surgeons. Of the 247 fresh patella fractures, 30 were wired by the method described here. This study does not include ligamentous tear about the patella without fractures.

The selection of wiring cases had one prerequisite. The main fragments had to show ¼ inch or more separation. All fractures showing less than ¼ inch separation of main fragments were treated by closed reduction and cast.

A comparative study was carried out using patellectomy, partial patellectomy, screw fixation, Kirschner wire, and various methods of wiring, suturing, or turnbuckle clamps.

METHOD

A Kocher incision is used over the knee and reflected upward. The rent of the capsule, or the area where the anterior capsule is relaxed due to separation of the fragments, is located and opened transversely. The quadriceps expanded from the lateral border to a distance of one inch from the fracture site of either pole. Following wound débridement the edges of the fractured fragments are curetted and approximation is checked for smooth closure. Using a No. 1 bit, a hole is drilled transversely across the main fragments, ⅓ inch from the fractured end and slightly eccentric to the frontal plane. Care is taken that the drill holes do not encroach on the posterior patella articular cartilage (Fig. 1). By use of an awl, the No. 22 stainless steel wire is passed through the two drill holes in a loop manner and the free end is then passed through the mid-frontal attachment of the quadriceps on the patella in a circumferential manner and then in the same way through the patella tendon. In each instance, the wire must hug the circumferential border of the patella at its mid-portion. The wire ends are then crossed at the place of bony insertion. As the wires are made taut by the assistant, the surgeon inspects the smooth gliding posterior surface of the patella for the anatomic reduction, and then several twists of wire are made by the assistant for fixation. The free wire ends are cut, leaving a stump of ¼ inch. The wire ends must not infringe upon the articular margin of the patella. The capsule is sutured with No. 1 chromic catgut, with 000 black silk to the skin.

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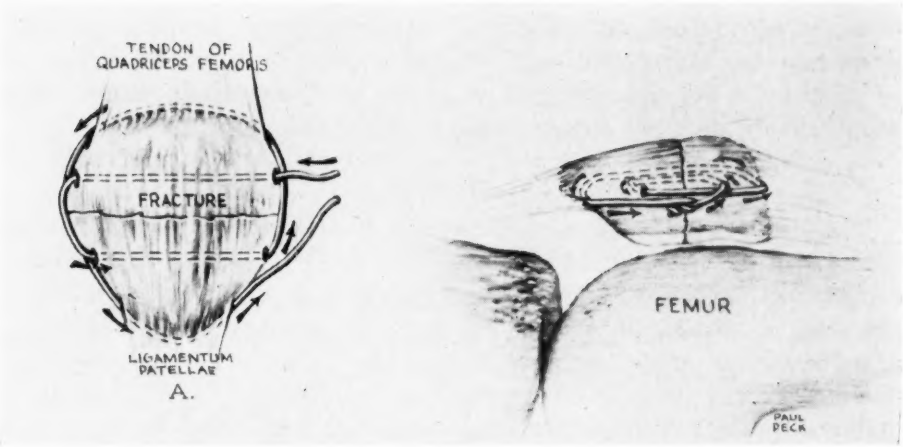

Fig. 1.—Position of drill holes and direction of wiring. (From the Orthopedic Service of the United States Marine Hospital, Stapleton, Staten Island.)

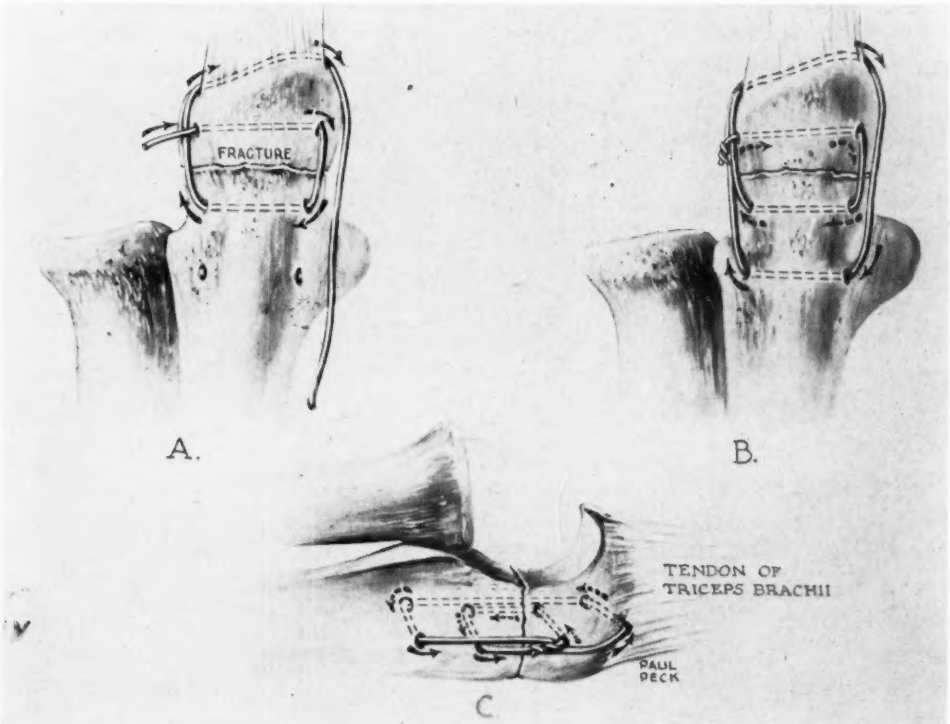

Fig. 2.—Wiring of olecranon. *A*, Method of passage of 22 gauge stainless steel wire through juxta fracture site; *B*, twisting and fixing of wire loop; *C*, lateral view of position of drill holes and direction of wire. (From Michele, Olecranon Fractures, J. Bone & Joint Surg., January, 1948.)

A cast is applied from the groin to the toes with the knee in mild flexion. The cast is split in three weeks and quadriceps and straight leg raising exercises are carried out. At the end of the fourth week, whirlpool, active, and passive exercises are carried out. Weight-bearing with guiding flexion of the knee on crutches is begun. Flexion to a right angle is possible within five weeks postoperatively, and full motion at the seventh to the eighth week.

RESULTS

The pertinent results of this method of treating fractured patellae revealed (1) snug, smooth, and sturdy closure of the fracture; (2) reduction of complications following such fractures, as well as greater ranges of motion when some limitation of motion was present than with other methods; (3) marked reduction of the number of days hospitalized as well as convalescing days, early ambulation, and nursing care requirement; (4) the final healed patella more nearly simulating the normal patella than following other methods.

This method reduced the hospital cost as well as absenteeism almost one-half in comparison with former methods.

THE USE OF CANCELLOUS BONE GRAFTS FOR SMALL DEFECTS OF SKULL AND BROW REGION

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IN THIS series there are five cases. In one case the calvarium proper was involved. In three there were defects of the frontal region of the skull and the brow. In one there were defects of the brow and nose.

The causes of these defects are interesting. One was the result of war injury, which involved the temporal bone in the region of the anterior attachment of the temporalis muscle. The remaining four are typical civil injuries. One was the result of the explosion of a truck tire. The other three were sustained in automobile accidents. In all five cases compound fractures with underlying brain damage resulted. These patients underwent immediate débridement in other hospitals and were sent here for repair. In only one case was there any appreciable tissue loss. All of the cases of injury to the brow region were complicated by fractures into the frontal sinus, and at the time of the bone graft it was seen that the sinuses had been obliterated.

The operative results of these cases were good. There was complete absence of pulsations in the defects within two to four weeks. Palpation demonstrated the fact that all defects were solid. There was good contour to the skull and to the brow. These patients were followed repeatedly by roentgenograms. During the first six weeks there was absorption of calcium in the grafts. At the end of three to four months the calcium was replaced. In areas where cancellous chips were used, there was a mottled appearance. The postoperative courses of these patients were uneventful. There were no signs or symptoms of any increase of intracranial pressure.

METHOD

The edges of the defects in the skull were carefully exposed and the bone was freshened with a small dental chisel. When the dissection was carried over the defect in bone, care was taken not to damage the dura. When this dissection was finished, invariably the dura was seen to fall back below the edges of the bone. The iliac crest was exposed and cortical portion laid back with the saw. Sufficient cancellous bone was removed and cut into small triangles. These were fitted into the defect in the manner described by Mowlem.[2, 3] It is very easy to secure the proper contour to the calvarium in this fashion. However, it has been found that this method is more difficult to use in the brow region. For the defect in this area two curving blocks of cancellous bone are used and shaped

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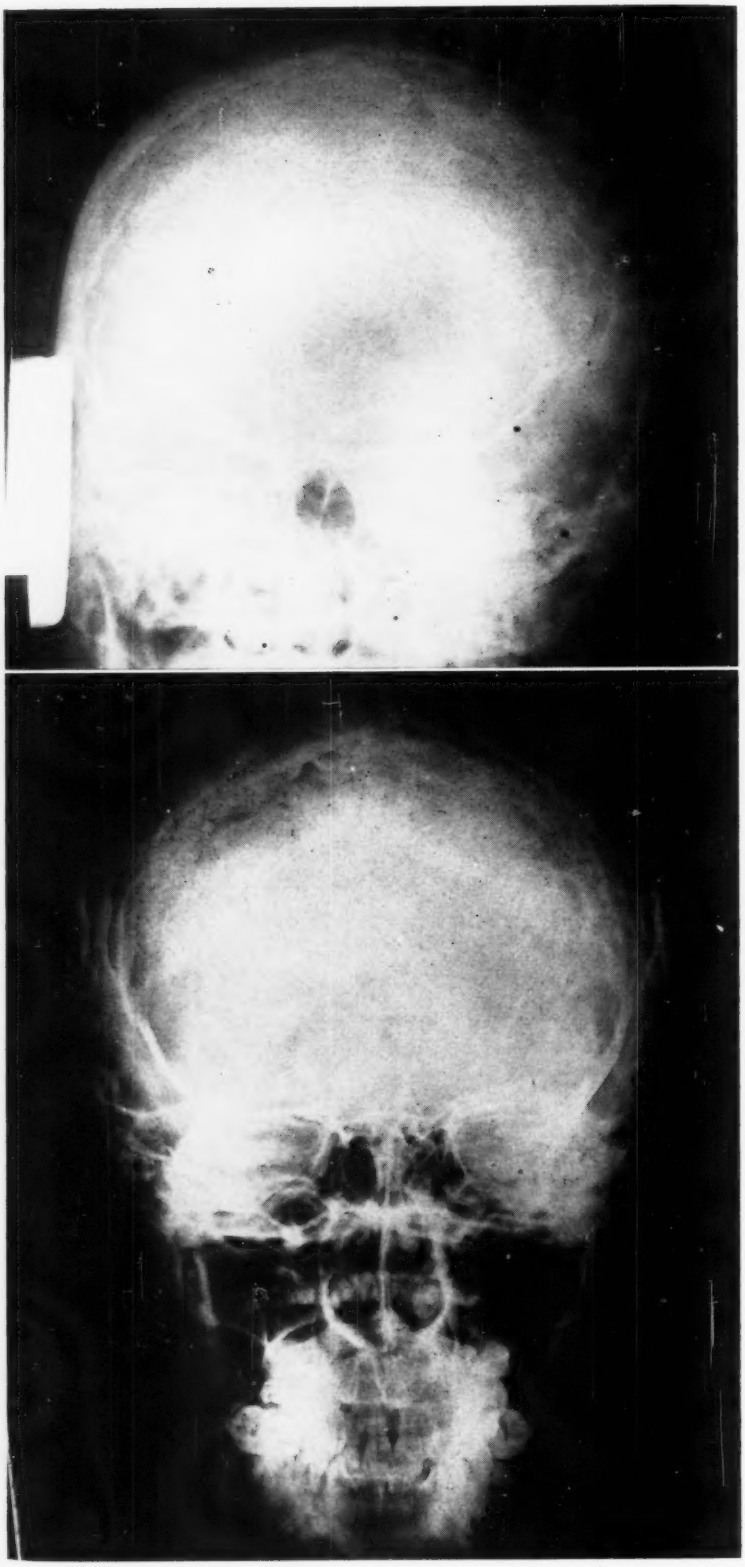
*Lieutenant Colonel, Medical Corps, Army of the United States, inactive.

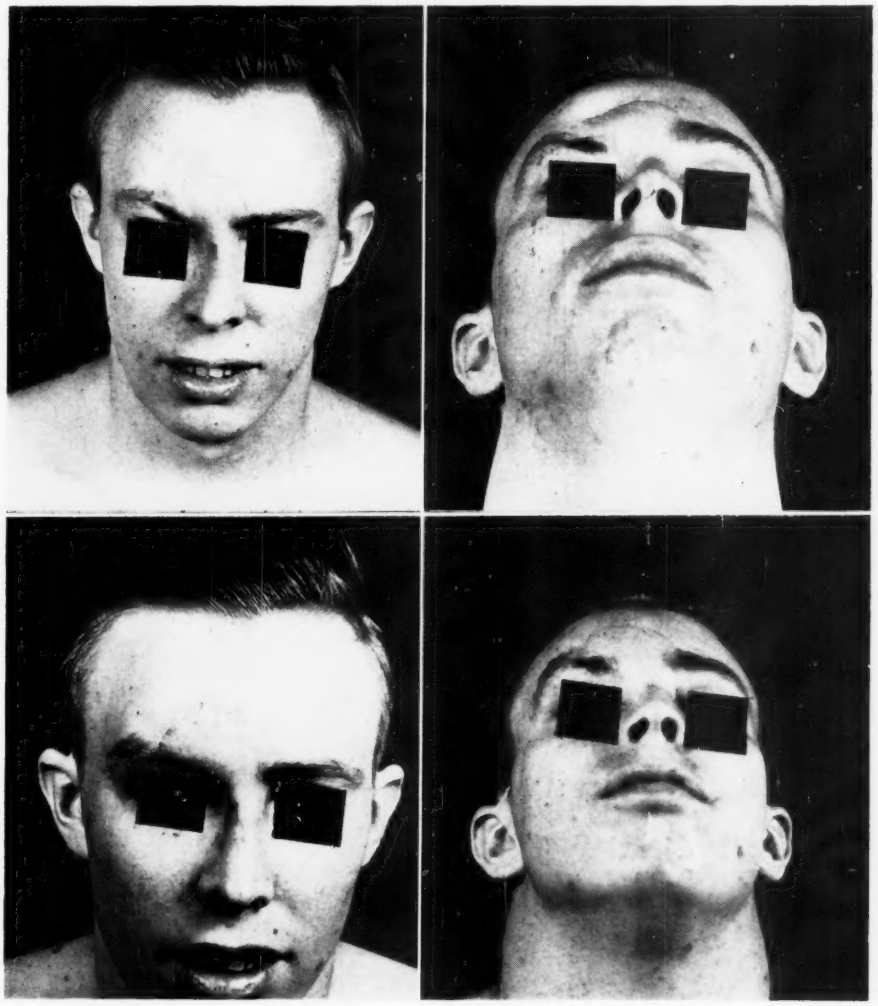


A.

B.

Fig. 1.—*A*, X-rays showing defects; *B*, after bone graft.

to resemble the normal supraorbital ridge. These are inserted in the bed formed by the subperiosteal exposure of the frontal bone in the region of the defect. Small chips are placed around the graft to complete the filling of the deformity. After proper contour is secured a dental modeling compound impression of the area is made. It is allowed to harden and is reapplied with firm pressure. This firm pressure by a smooth surface prevents any irregularities and maintains the contour. This is worn for three to four weeks.



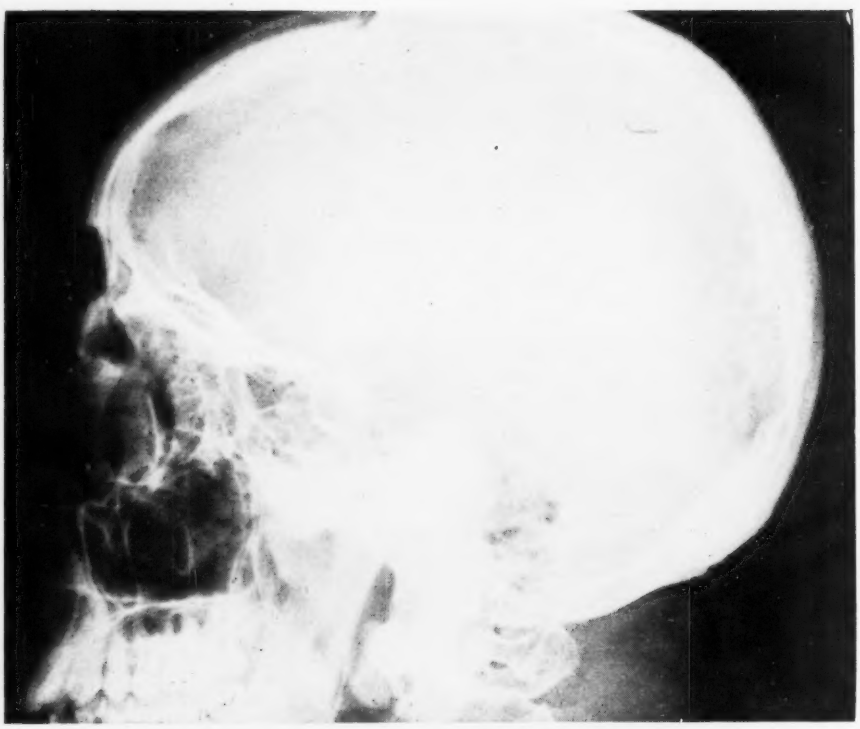
A.

B.

Fig. 2.—*A*, Injury caused by exploding truck tire; defect of right supraorbital region and frontal bone. *B*, After bone graft.

DISCUSSION

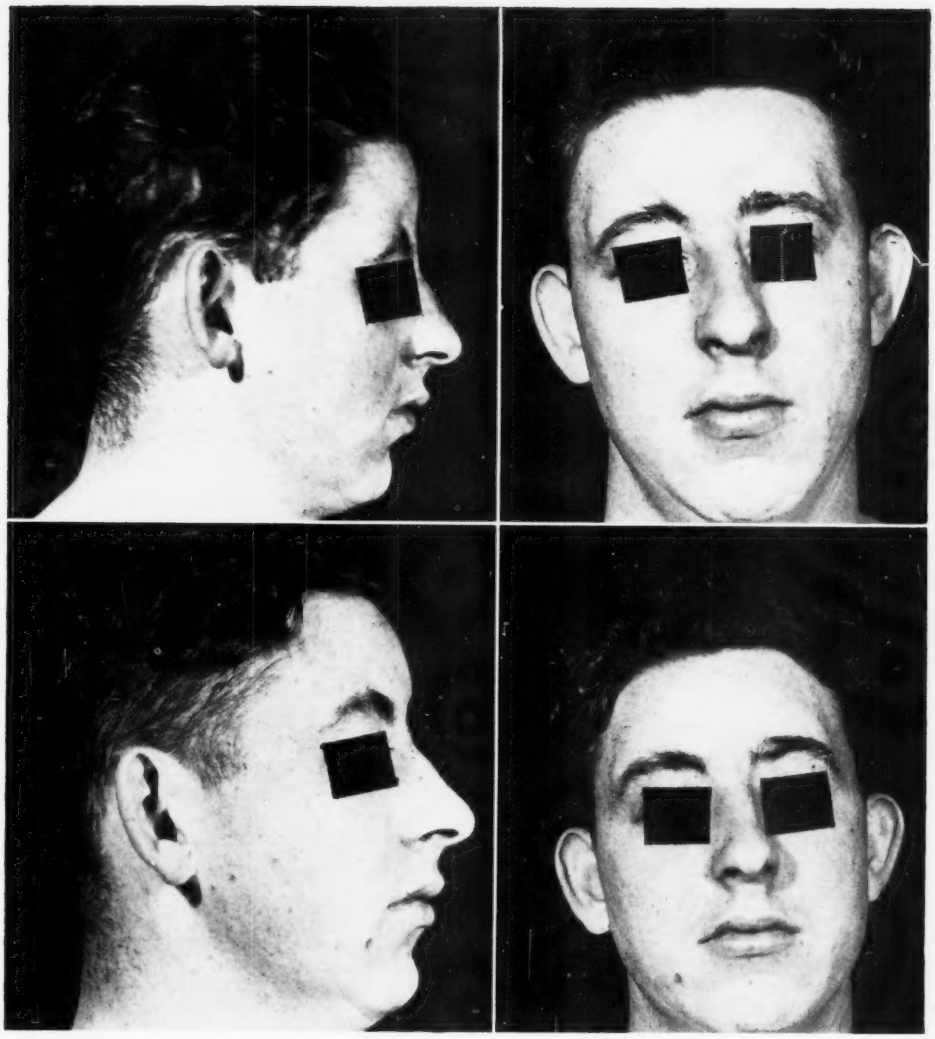
It is felt that cancellous bone is readily adaptable to repair of small defects of the skull, especially in the brow region where it is difficult to contour any foreign material such as tantalum or acrylic. In view of the superior resistance



A.

B.

Fig. 3.—X-rays of, *A*, lateral view showing defect; *B*, view showing grafts.



A

B.

Fig. 4.—*A*, Compound comminuted fracture of frontal bone, suffered in an automobile accident; condition after débridement, defect of both supraorbital ridges and frontal bone. *B*, Bone graft by using curved blocks to simulate the supraorbital ridges and chips in the frontal bone defect; incision through previously existing scars in the eyebrows.

A. *B.* *C.*

Fig. 5.—Severe compound injuries in the right supraorbital and frontal regions, *A* and *B*. Multiple fractures of maxilla, mandible, and nasal bones. There was considerable tissue loss in the region of the right eyebrow. *C*, Cancellous bone graft in the nose and on supraorbital ridge; whole thickness skin graft above hairline to relax the skin above the eyebrow and to lower that structure.

of cancellous bone to infection, which is always a hazard when working near the nasal sinuses, it is felt to be markedly superior to any foreign material no matter how inert.

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COMPOUND TRANSVERSE FRACTURE OF THE MAXILLA

Report of a Case With Zygomatic Fixation

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(From the Otolaryngologic and Plastic Surgical Section, Hospital San Juan de Dios)

According to Adams,* until a few years ago, some type of extraoral appliance was generally employed in cases of severe, compound transverse fracture of the maxilla. Since then, however, open reduction and fixation by wiring of the fracture to the neighboring unfractured bone has been performed in most cases. A simple, new operative procedure, used in the case to be reported, has been devised whereby the floating fracture of the maxilla is attached to the zygomatic arch with tantalum wire. It requires no plaster head caps or cumbersome intraoral or extraoral appliances, and is not uncomfortable for the patient.

REPORT OF A CASE

M. V. G., an edentulous, 71-year-old man, was admitted to the Hospital San Juan de Dios in San Jose, Costa Rica, on March 6, 1945, with a compound transverse fracture of the maxilla. Thirty-six hours before admission, he had been kicked by a horse, the ridge of the horse's hoof striking him immediately below the nose, producing a semilunar, lacerated, contused wound extending through all layers of the upper lip. The alveolar edges of both superior maxillas were avulsed. The palatine bone was thus freely movable and resting upon the tongue (Figs. 1, 2, and 3).

Under an intratracheal anesthetic a small drill hole was made in the superior alveolar process just above the former site of the second premolar tooth. A tantalum wire was passed through this hole and the end brought outward over the alveolar ridge. A long, slightly curved, Reverdin needle was then inserted immediately above the anterior end of the zygomatic arch and pushed downward, forward, and medially to enter the mouth at the gingivolabial fold. One end of the wire was then threaded through the needle and brought out superior to the zygomatic arch. The Reverdin needle was again inserted through the same hole in the scalp and passed laterally to the zygomatic arch to enter the mouth at the gingivolabial fold. The second end of the wire, which passed over the alveolar process, was then threaded through the Reverdin needle and brought outward. The two ends of the wire were then passed through a button 1 cm. in diameter. The same procedure was performed on the opposite side (Figs. 4, 5, and 6). A drill hole was made on each side of the midline of the hard palate 5 mm. apart and a third wire was passed through these holes and fixed to the lamina perpendicularis. This wire, however, did not contribute to reduction of the fracture as the thin lamina perpendicularis will not withstand such tension (Figs. 5 and 6). The fracture of the left infraorbital ridge was elevated into normal position (Figs. 2 and 5). Both maxillary sinuses were then packed with iodoform gauze to restore the normal contours of their walls. The soft tissues of the lip were sutured in three layers. The lateral wires were then tightened through the buttons to maintain reduction of the fracture of the superior maxilla (Figs. 4, 5, and 6).

Preoperatively, the patient received antitetanic and antigangrene serum. Following the operation he was given sulfadiazine, 1 Gm. every four hours, and penicillin, 20,000 units every four hours, for five days. On the first postoperative day a transfusion of 300 c.c. of whole blood was given. The patient was fed through an intranasal catheter for eight days.

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*Adams, W. M.: Internal Wiring Fixation of Facial Fractures, Surgery 12: 523-540, 1942.

Fig. 1.

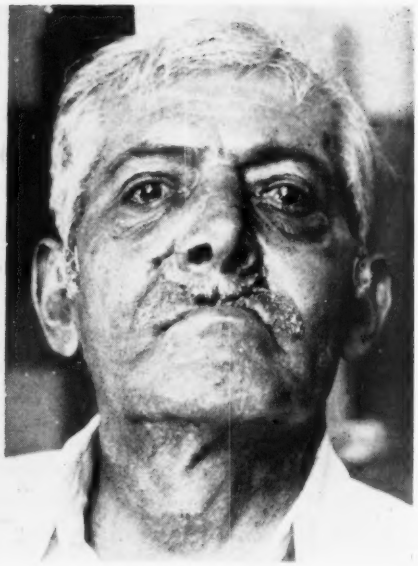


Fig. 4.

Fig. 2.

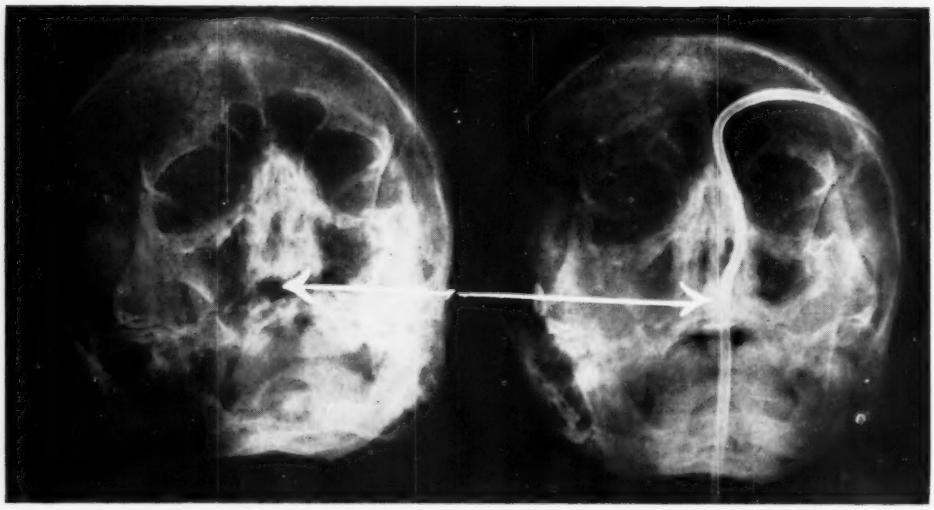


Fig. 5.

Fig. 3.

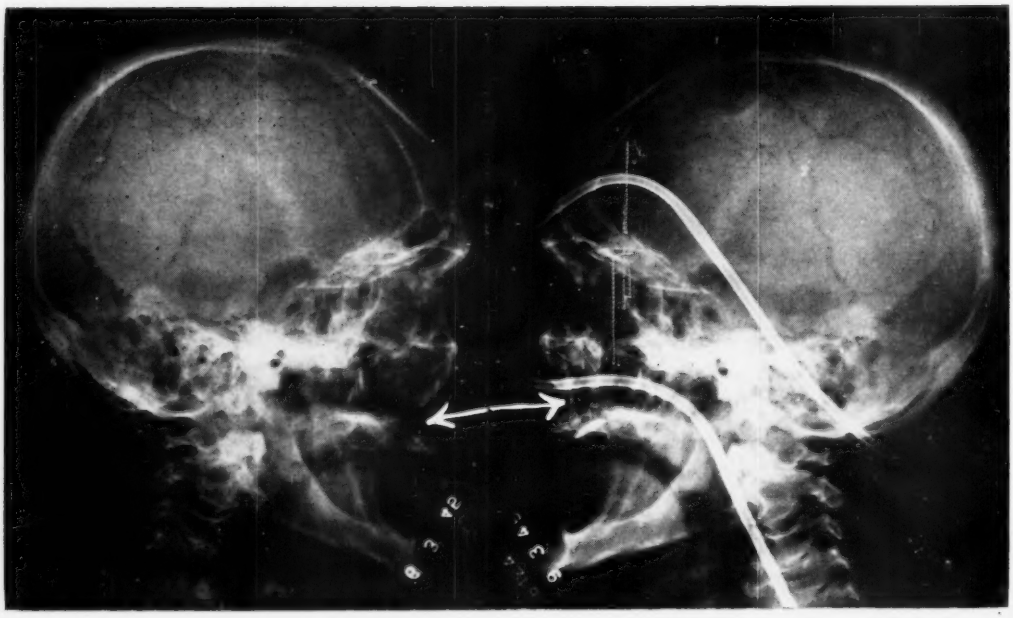
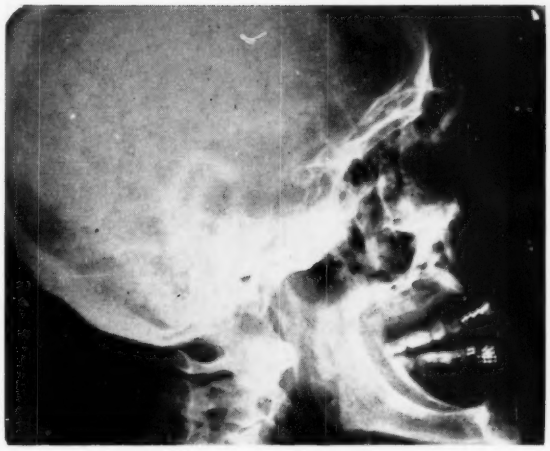


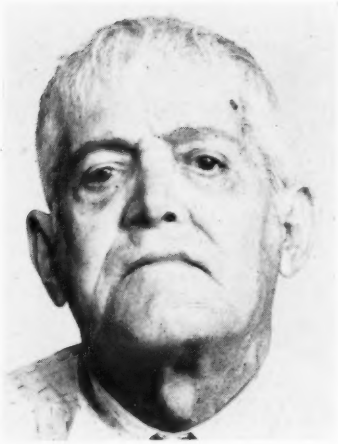
Fig. 6.

(For legends see opposite page.)



A.

B.



C.

Fig. 7 *A*, *B*, and *C*.—Final results two years after the accident.

Fig. 1.—Photograph of patient showing extent of injury.

Fig. 2.—Roentgenogram showing anterior view of complete transverse bilateral fracture of the maxilla; note also fracture of the lower orbital arch.

Fig. 3.—Roentgenogram showing lateral view of the fracture; note downward displacement of the palatine bone.

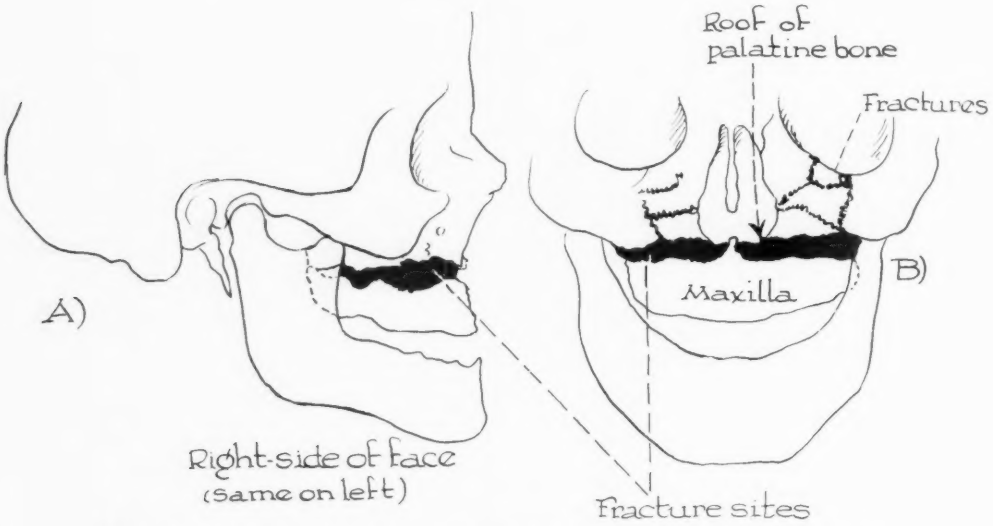
Fig. 4.—Photograph of patient twenty-five days after the operation; note buttons where the wire was twisted over the zygoma.

Fig. 5.—Roentgenogram taken after reduction of the fracture; note palatine bone in normal position, also wires and buttons in place.

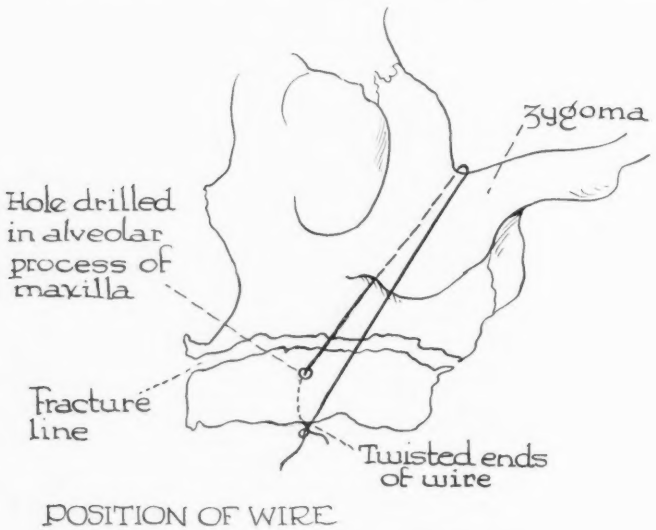
Fig. 6.—Lateral view of roentgenogram taken following reduction of fracture.

The antral packs were removed on the fourth postoperative day. The inflammatory edema subsided by the ninth postoperative day and the patient left the hospital on the fifteenth postoperative day. The wires were removed on the twenty-fifth postoperative day.

The patient made an uneventful recovery. Reduction of the fracture has been maintained. The patient has now worn a dental prosthesis approximately for two years without difficulty. At the age of 74 years he is still dealing with horses.



Drawing 1.—*A*, Lateral view of fracture site; *B*, front view of fracture site.



Drawing 2.—Position of wire in edentulous patient.

COMMENT

This procedure is presented because it is simple to perform and comfortable for the patient. In patients who have teeth, the procedure is further simplified by the elimination of the use of drill holes since the teeth may be utilized for fixation of the wires.

THE EFFECTS OF THE SUPINE POSITION UPON THE VENTILATION OF THE LUNGS OF DOGS

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(From the Department of Physiology, Harvard School of Public Health)

SOME years ago we were struck by the abnormal appearance of lungs of dogs kept under deep anesthesia and held supine for some hours. The lower lobes, dorsally and extending variable distances toward the apices, were congested and liverlike in appearance. It was apparent that blood cells had ceased to move in the capillaries of these dependent parts, though lung edema was not an apparent eventuality so far as we could judge.

A little later, Krogh,[1] in 1924, emphasized the role of stasis as a vascular problem, and, as time passed, this conception took more and more hold upon workers in this laboratory. Briefly stated, the idea was that in dependent parts of the pulmonary circulation in deeply anesthetized dogs, breathing poorly, the blood movement became unduly slow, plasma in small amounts moved out of the capillaries, and the capillary circulation was blocked by packed red cells which lacked plasma to float them along.

In the lungs, the appearance resulting from this phenomenon is a reddish solidity of dependent parts. How serious to a patient such an experience may be is hard to say. As anesthesia passes off and the circulation becomes normally active, it would be our opinion that the stasis of red cells is slowly broken up and normal circulation is re-established.

Many people think of edema as an inevitable result of circulatory block, but this idea is obviously wrong unless blood continues to be forced against a barrier. In the case of stasis, wherever it occurs, the circulation stops, and such small amounts of plasma as may be present in the capillaries of the region may escape. But once this has happened, the area is dry. The production of edema requires an active, or reasonably active, supply of blood. It is a progressive process. When the circulation to a part ceases, then only that plasma in the capillaries at the moment can become extravascular, and this is the reason that stasis in pulmonary capillaries does not result in pulmonary edema.

Our first observations were made in the course of other experiments in which dogs anesthetized with nembutal were supine over many hours and entirely immobile. Invariably there was a liverlike solidification of the lower lobes extending up along the spine where lung movement was negligible or absent. When such regions were sectioned with a razor blade they were bloody, but the frothy points which one associates with lung edema were absent.

Becoming curious in regard to the situation, as it involved the capillaries, we injected intravenously a suspension of fine particles of graphite into dogs early in anesthesia, and in others after some hours. These experiments were reported by Drinker[2] in 1945. They showed that when an animal was in the

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early stages of anesthesia, graphite particles were widely and uniformly distributed through the lungs; but after some hours in the supine position, when the lower lobes posteriorly were red and solid, then injected graphite particles did not enter these areas, indicating blockage of pulmonary capillaries.

The experiments reported in this paper have been designed to discover how far dependent, apparently solid parts of the lungs fail to be reached by air when the animal is breathing normally. It is our belief that the primary condition causing blockage of air entrance into the alveoli is vascular. This conception will be clearer after presentation of experiments and our explanation found in the discussion.

EXPERIMENTAL

Under nembutal or sodium veronal anesthesia, a tracheal cannula with three openings was introduced, as shown in Fig. 1. This cannula, *E*, enters the trachea of the dog at *F*, and two wide ends permit the entrance and exit of aerosol introduced into a bottle, *B*, by means of a simple atomizer through tube *A*. The bottles used were of 4 liter capacity, and into *B* a lead, *C*, delivers a constant stream of oxygen. The stopper, *H*, in bottle *I* is of loose cotton to avoid the development of pressure and, at the same time, to minimize leakage of the aerosol into the laboratory air.

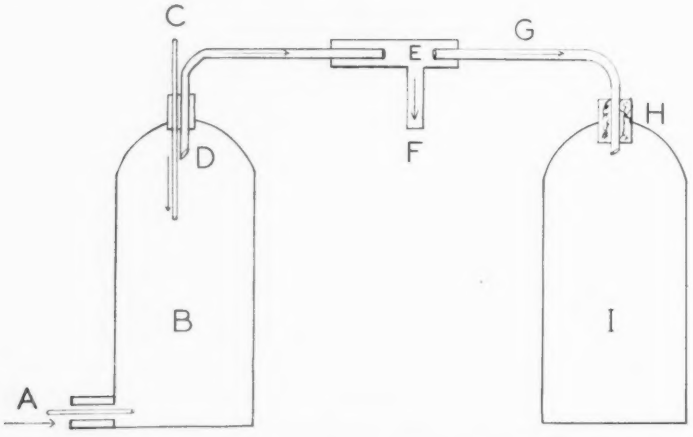


Fig. 1.—*A*, inlet from atomizer supplying vaporized dog serum plus T-1824; *B*, 4 liter bottle; *C*, tube for supplying oxygen or oxygen-carbon dioxide mixtures; *D*, line to tracheal cannula, *E*; *F*, entrance of cannula into trachea of dog; *G*, glass tube to remove excess aerosol; *H*, cotton plug filtering aerosol and preventing development of pressure in reservoir bottle, *I*.

The aerosol employed had the following composition: 200 c.c. of a 2.5 per cent solution of T-1824 in 0.85 per cent salt solution added to 300 c.c. fresh dog serum. The final concentration of T-1824 was thus 0.5 per cent and of dog plasma protein about 3 per cent. The aerosol was made by putting this solution in an atomizer and using compressed air to produce the mist. This resulted in a beautiful blue vapor, which was blown into the 4 liter glass bottle, *B*, from which the dog breathed naturally. Excess vapor passed into another large reservoir, *I*, connected with the opposite opening in the cannula and stoppered loosely with cotton. This last measure was found necessary since

without it appreciable amounts of the aerosol could be seen in the air of the laboratory, and after a number of experiments in which blue was noticed on blowing our noses, some degree of sensitization began to appear, and this had to be checked promptly. The reason for adding serum to the dye solution resides in the fact that the addition of protein to T-1824 solutions prevents the dye from being absorbed from the alveoli, whereas simple water solutions are absorbed at once, mainly into the pulmonary capillaries, and distributed promptly all over the body (Drinker and Hardenbergh,[3] 1947). The addition of the serum anchors the dye aerosol in the alveoli reached by it.

A further interesting fact occurred in the first three experiments. After breathing the aerosol for twenty to thirty minutes, the animal died of anoxia. It was some time before we realized that oxygen under these circumstances was so far replaced by water vapor as to produce inevitable anoxia and death. When oxygen or an oxygen-carbon dioxide mixture was bled into the system through tube *C* (Fig. 1), the difficulty ceased at once.

At the close of each experiment the animal was bled to death; the trachea was then clamped, and the lungs removed without permitting them to collapse. Colored photographs were made promptly and gave a very graphic picture of the distribution of the blue aerosol, which obviously entered alveoli that had remained open. Since reproduction of colored illustrations is unduly expensive, outline drawings have been made from them, and areas blue in color have been stippled as seen in Figs. 2, 3, 4, and 5. Clear regions thus mean parts of the lungs where alveoli were not reached by the aerosol.

A typical experiment was as follows:

Nov. 2, 1945, dog weighing 10.2 kilograms

9:20 A.M.	6 c.c. of 5 per cent nembutal, intravenously
9:30.	3 c.c. of 5 per cent nembutal, intraperitoneally
10:05.	50 c.c. of Ringer's solution, intravenously
12:00.	50 c.c. of Ringer's solution, intravenously
1:05 P.M.	Animal began to breathe blue aerosol, made as described
1:10.	50 c.c. of Ringer's solution, intravenously
2:20.	1 c.c. of 5 per cent nembutal, intravenously
3:25.	50 c.c. of Ringer's solution, intravenously
3:55.	Dog bled to death, lungs removed, and colored photographs made twenty-five minutes after death

The results of this experiment are shown in Figs. 2 and 3. Fig. 2 shows the posterior aspect of the lungs, and it is at once apparent that very little blue has entered the lower lobes except high up. This animal had been immobile on his back from 9:20 A.M. to 1:05 P.M., and then inhaled the blue aerosol until 3:55 P.M. The result indicates that something over three hours in the supine position causes a considerable degree of alveolar blockage. Fig. 3 is a view of the same lungs from the right side.

Figs. 4 and 5 are again posterior and left lateral views of a dog anesthetized with nembutal and supine from 9:50 A.M. to 3:25 P.M. In this case, except for two short intervals the animal breathed a mixture of 9.46 per cent

carbon dioxide and 90.54 per cent oxygen. The aerosol was breathed from 1:30 P.M. to 3:25 P.M., and was produced by the usual blast of compressed air. During this time, the oxygen-carbon dioxide mixture was blown into bottle *B* through tube *C*. Breathing ,due to the carbon dioxide, was deeper than normal.

Fig. 2.

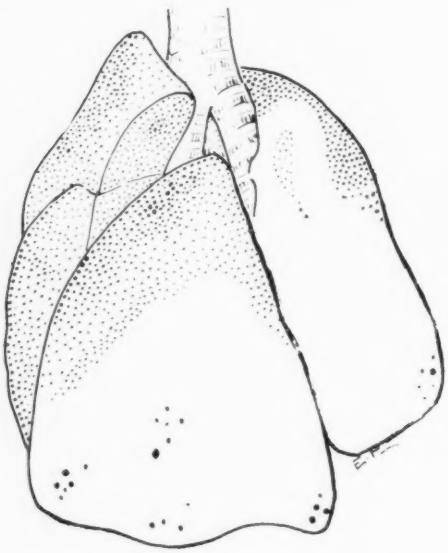
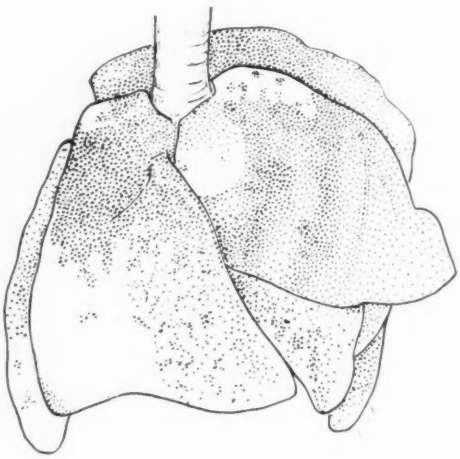


Fig. 3.



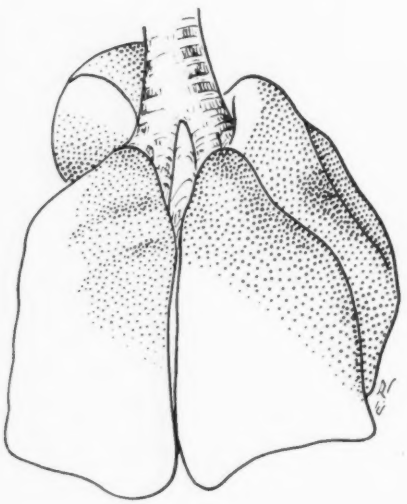


Fig. 4.

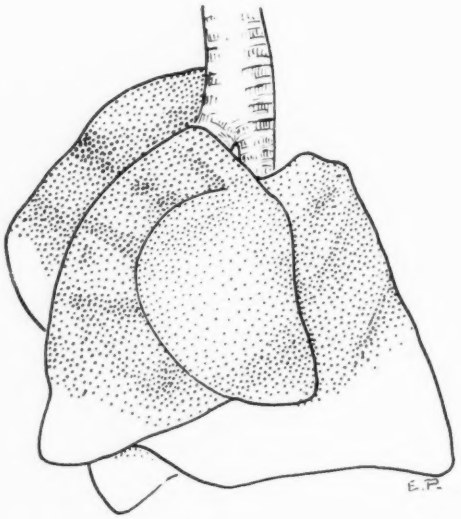


Fig. 5.

Fig. 2.—Posterior view of lungs of a dog which inhaled oxygen and a dog serum T-1824 aerosol for 2 hours and 50 minutes after 3 hours and 45 minutes in supine position under nembutal anesthesia. The areas covered by black dots indicate those parts reached by the insoluble blue aerosol.

Fig. 3.—Right lateral view of lungs from dog in Fig. 2.

Fig. 4.—Posterior view of lungs of a dog which inhaled carbon dioxide oxygen and serum T-1824 aerosol for 2 hours and 25 minutes after lying supine for 3 hours and 35 minutes under anesthesia by nembutal. The areas covered by black dots are those entered by the blue aerosol.

Fig. 5.—Left lateral view of lungs from dog in Fig. 4.

but was slower than one is accustomed to seeing when using such mixtures. The results indicate marked failure of the aerosol to reach the posterior parts of the lower lobes. Possibly a more vigorous response to the carbon dioxide would have lessened this effect; but the fact remains that, even with a fair degree of increased breathing, alveoli in these dependent and relatively immobile areas are not reached by the aerosol.

DISCUSSION AND CONCLUSIONS

This paper concentrates upon the failure of air to enter alveoli in certain parts of the lungs placed at a disadvantage as a result of prolonged fixation in what for the dog is certainly an abnormal position. Dogs do not sleep or rest flat upon the back. But it is equally true that except under anesthesia, or as a result of injury, man does not remain in a fixed position during sleep. In sleep he moves frequently, with the result that stasis in the pulmonary capillaries in any one region is avoided. In experiments through many years, invariably, whether upon anesthetized dogs or other animals apparently in the best of health, lung conditions like those we have described have been seen repeatedly. Their significance when applied to prolonged surgical operations in man cannot be estimated other than to point out that after long anesthesia every patient is left with a circulation and ventilation of the lungs which are not normal and must be corrected before the patient is in normal health once more. That these blocked pulmonary capillaries begin again to transmit blood when healthy animals recover from anesthesia and begin to move about is certainly the case. But in old and feeble persons, reluctant to cooperate, and stoutly opposed to being moved or bothered in any way, it is not easy to accomplish changes in position which may ward off serious complications in the lungs. It was our idea that occasional periods of inhalation of 93 per cent oxygen and 7 per cent carbon dioxide might be an easy method of avoiding atelectasis. This is by no means certain unless the anesthesia is short and the periods of inhalation are begun early in the operation.

It is natural to ask why healthy anesthetized dogs, kept in one position and quite immobile, experience stasis in certain pulmonary capillaries, accompanied by blocking off of alveoli and atelectasis. As has been pointed out, the supine position is an unusual one for the dog and, lacking anesthesia, never maintained except for short periods. When, as in these experiments, the animal is supine and immobile over some hours, the dorsal and dependent parts of the lungs are pressed against the posterior part of the thorax, which in turn is supported by a rigid animal board. Thoracic movement under these conditions is in the sternal part of the chest, which is the free part. Under normal circumstances the lungs contain a large amount of blood in a meshwork of interconnecting capillaries. With a relatively slow blood flow, all that is necessary to achieve adequate oxygenation of the blood, there is settling of blood in the dependent parts of the lungs which lie against the most rigid part of the chest. In our opinion, this settling, coupled with little movement of the alveoli, overfills the capillaries and after a time there is blockage of flow with leakage of a

small amount of plasma into the alveoli and possible eventual blockage of bronchioles. Dock[4] and Harrison,[5] in 1944, related bed rest to the development of pulmonary complications in bedridden patients, particularly those with cardiac disease. In the case of healthy dogs under barbiturate anesthesia, it is probable that cardiac output was reduced as compared with the unanesthetized state and this factor would of itself tend to promote stasis and alveolar collapse. The same localization of stasis to the sternal margins of the lungs with subsequent alveolar collapse can be made to occur along these margins of the lungs if the anesthetized dog is placed prone instead of supine.

SUMMARY

1. The development of stasis and blockage of pulmonary capillaries in dogs anesthetized with barbiturates and held supine for some hours is described.

2. The effect of this stasis, which occurs essentially in dorsal and dependent parts of the lungs, is to bring about slight transudation of plasma into the alveoli with blockage of air entrance. Atelectasis slowly develops.

3. Much experience has shown that normal dogs so treated and allowed to recover from the anesthetic (nembutal) usually show no signs of trouble from the lung condition which must have been present when anesthesia terminated and consciousness returned. This does not preclude the fact that in every case of prolonged anesthesia or immobility in a single position, the animal or man so treated must dispose of an abnormal pulmonary condition before normal health is attained.

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POSTERIOR CISTERNAL DRAINAGE OF THE HYDROCEPHALIC THIRD VENTRICLE (POSTERIOR THIRD VENTRICULOSTOMY)

Preliminary Note

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SEVERAL palliative procedures have been advised for the operative treatment of noncommunicating internal hydrocephalus in cases where the cause of the obstruction cannot be removed, for example, by radical operation of intraventricular tumors, new growths of the middle or posterior fossae, and pineal tumors.

From a historical standpoint we must mention Anton-Bramann's *Balkenstich* (puncture of the corpus callosum) "for draining the lateral ventricle toward the subdural space on the convexity of the cerebral hemisphere."

Dandy's anterior or lateral third ventriculostomy, opening the floor of the third ventricle toward the cisterna terminalis or cisterna fossae sylvii, and Torkildsen's drainage of the lateral ventricle toward the cisterna cerebellomedullaris by means of a rubber tube—these are the methods used today by the majority of the neurosurgeons as palliative operations for noncommunicating internal hydrocephalus.

So far as we know, no attempt has been made until now to try a ventriculostomy at the posterior end of the third ventricle, at the region of the recessus suprapinealis. Two factors seem to be in favor of such a procedure, namely, the frequently noticed enlargement of this recessus in cases of internal hydrocephalus, and the thinness of the wall of the recessus, which, according to the textbooks of anatomy, consists of ependyma only.

An expansion of the suprapineal recessus is often seen on pneumograms of a hydrocephalic third ventricle.

Chamberlain (Philadelphia), who described the downward displacement of the pineal shadow as an important symptom of internal hydrocephalus, explained it as caused by the bulge of the recessus suprapinealis.

The cistern adjacent to the suprapineal recessus is the cisterna venae magnae Galeni. The question arises as to whether or not an operative procedure can be devised which allows the drainage of the recessus suprapinealis toward the cisterna venae Galeni. It may be possible to reach these structures by an infratentorial approach.*

Main indications for posterior third ventriculostomy would be stenosis of the aquaeductus sylvii and inoperable tumors of the posterior fossa.

The new procedure may avoid inconveniences of the other methods, damage of the cerebral hemisphere in Torkildsen's operation, and hyperthermia in Dandy's third ventriculostomy.

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*A similar method has been described for the operation of infratentorial diverticulum of the ventricles by Pennybacker and Russell (J. Neurol. & Psychiat. 6: 38-45, 1943.) See also Perryman and Pendergrass, Am. J. Roentgenol. 59: 27-52, 1948.

Case Reports

TUMOR-FORMING AMYLOIDOSIS OF THE LUNG

Report of Case

Allan L. Haynes, M.D.,* O. Theron Clagett, M.D.,† and
John R. McDonald, M.D.,‡ Rochester, Minn.

AMYLOID deposits have been encountered in many parts of the body. The most familiar manifestation of amyloidosis is the extensive deposition of amyloid in organs such as the liver, kidneys, and spleen in the course of chronic suppurative disease. There have been increasingly frequent observations of amyloid in other organs either with or without preceding disease; consequently, amyloidosis has been divided into the following four types according to the classification of Reimann, Koucky, and Eklund[1]: (1) primary amyloidosis (systemic or atypical amyloidosis), which usually involves multiple sites in the mesodermal tissues such as heart, lungs, and skeletal muscle and usually is unaccompanied by antecedent disease; (2) secondary amyloidosis, which is characterized by deposition of the substance in the liver, kidneys, and suprarenal glands in the later stages of chronic suppurative disease; (3) tumor-forming amyloidosis, which is characterized by the formation of solitary masses usually in mesodermal tissues and commonly without antecedent disease as a possible etiologic factor, and (4) amyloidosis associated with multiple myeloma in such sites as lymphoid tissue, bone marrow, and in or around the joints.

The localization of the deposits of amyloid is by no means as sharply delimited as this classification would indicate; moreover, the association with previous disease is so inconstant that many instances of the disease cannot be placed in either of the first two categories. Tumor-forming amyloidosis is generally regarded as a type of primary or atypical amyloidosis.[2] An extensive consideration of the types of amyloid disease and of the surgical significance of localized amyloid deposits was presented recently by Weismann, Clagett, and McDonald.[3]

Tumor-forming amyloidosis has been observed in several parts of the body, among them the skin, tongue, larynx and trachea, urinary bladder, and urethra. According to Figi,[4] when amyloidosis occurs in the upper part of the respiratory tract the sites of involvement in order of decreasing frequency are the larynx, trachea, and pharynx. Up to 1944, six cases of amyloid tumor of the urinary bladder had been reported in the literature.[5] In these organs and in other sites, the amyloid tumors have occurred as more or less isolated masses lying in the subepithelial strata. In the lung, amyloidosis has occurred in the form

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of primary or atypical amyloidosis, and as such it always has been associated with amyloidosis in other sites such as the heart, gastrointestinal tract, and spleen.[6-11] Weismann, Clagett, and McDonald found reports of three cases of localized amyloid disease of the lung and added a fourth case of their own.[3]

We wish to report a case of amyloidosis in which the amyloid material formed a single tumor which caused obliteration of a bronchus of the right lung and collapse of the adjacent pulmonary tissue.

CASE REPORT

A retired man, aged 66 years, who had been an executive for a telephone company, was referred to the clinic on Nov. 21, 1946, for treatment of a tumor of the right lung. Three years before the patient came to the clinic he had had a "mild cerebral vascular accident" but he had recovered promptly and completely. At the time of this illness the systolic blood pressure had been 200 mm. of mercury but it had gradually decreased to 140 mm. as a result of treatment.

Seven weeks before the patient came to the clinic, he had noted for the first time a burning midepigastric sensation in the course of exertion. This pain, or sensation, was not associated with the ingestion of food, it did not radiate, and it was relieved by rest. In subsequent weeks, this sensation seemed to be induced by lesser degrees of exertion and when he came to the clinic it could be elicited by his walking one block. A cough, productive of minimal quantity of sputum, had been noted about six weeks previously. The sputum never had been bloody. Coincidentally, a mild shortness of breath had appeared and had been present at all times. In the ten weeks before the patient came to the clinic, weight had declined from 154 to 142 pounds (69.9 to 64.4 kilograms).

Three weeks before he came to the clinic, a roentgenographic examination of the thorax had disclosed a tumor of the right lung. Electrocardiograms and roentgenograms of the stomach and colon had not revealed any abnormality.

When the patient was examined at the clinic he was rather well nourished and did not appear to be in distress. The systolic blood pressure was 145 mm. of mercury and the diastolic pressure was 90 mm. The pulse rate was 96, and the oral temperature was 99.4° F. Physical examination of the thorax did not disclose any abnormality. The thyroid gland was slightly enlarged and was described as nodular. A fine tremor of the hands was discovered. The results of the remainder of the physical examination were essentially negative.

The blood and urine were approximately normal and the result of a flocculation test for syphilis was negative. Roentgenographic examination of the thorax revealed an obstructive lesion of the bronchus of the middle lobe of the right lung and atelectasis of the lobe. On Nov. 25, 1946, the basal metabolic rate was +30 per cent. The administration of compound solution of iodine in doses of 10 minims (0.6 c.c.) three times daily was begun. On December 12, the basal metabolic rate was +25 per cent.

Bronchoscopy, which was performed on December 5, did not disclose a tumor mass in the bronchus of the middle lobe of the right lung. Microscopic examination of secretions obtained from the bronchus did not disclose any neoplastic cells. On December 9, bronchography disclosed a filling defect of the bronchus of the middle lobe.

Thyroidectomy was performed on December 16. The removed portion of the thyroid gland weighed 22 Gm. and contained a single degenerating adenoma. Subsequently, the basal metabolic rate gradually decreased until it was −10 per cent on Jan. 14, 1947. At that time, the dose of compound solution of iodine was reduced to 5 minims (0.3 c.c.) daily.

On Jan. 28, 1947, the right side of the thorax was exposed by making a posterolateral incision and resecting a portion of the sixth rib. A very hard tumor mass was felt in the middle lobe of the right lung, and it was noted that this lobe was completely airless. On palpation, the mass had all the characteristics of a malignant lesion; therefore, the right lung was resected and the right phrenic nerve was interrupted completely. A transfusion of 500 c.c. of whole blood was administered in the course of the operation.

Pathologic examination of the right lung disclosed a stony hard mass 6 cm. in diameter in the middle lobe (Fig. 1). The tumor was mottled gray and black in color, and it was firmly embedded in the surrounding lung tissue. The bronchus of the middle lobe passed directly into the mass and was completely occluded by it. It was impossible to pass a small probe into the bronchus within the tumor. The tissue of the middle lobe around this mass was completely collapsed; the lobe was about one-half its normal size. Microscopic examination of fresh frozen sections of the mass that had been stained with polychrome methylene blue disclosed a dense infiltration of a homogeneous bluish material in the walls of blood vessels, alveoli, and bronchi.

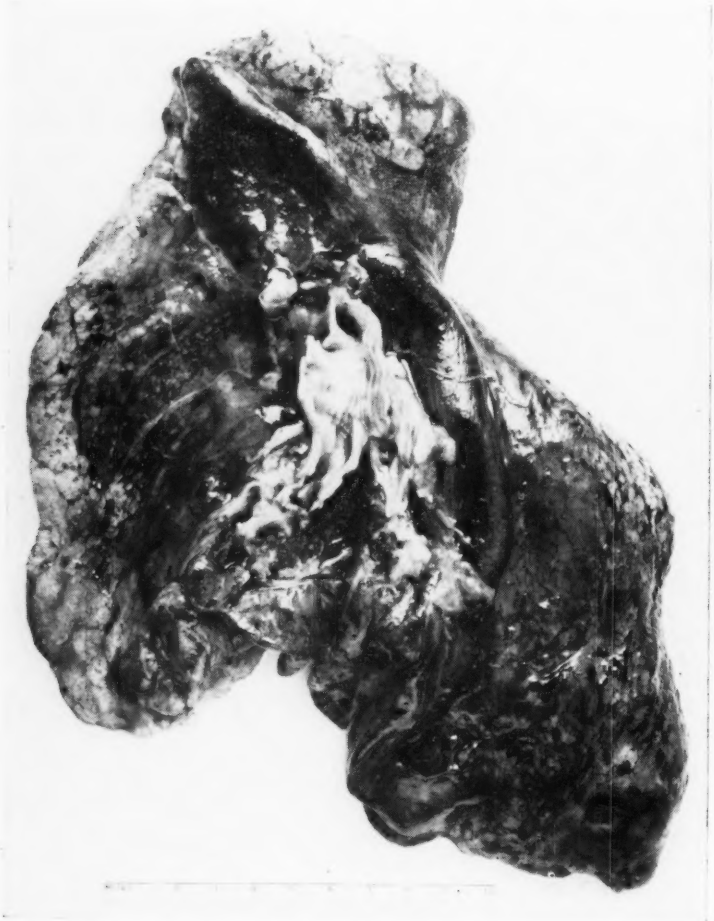

Fig. 1.—Amyloid mass in the middle lobe of the lung surrounding and occluding the middle lobe bronchus near its origin. The adjacent tissue of the middle lobe is airless and reduced in volume.

Sections that had been fixed with alcohol and stained with hematoxylin and eosin showed extensive deposition of homogeneous pink-staining material which seemed to be laid down primarily in the walls of small blood vesssels and in the interalveolar septa; to a lesser extent, the material was seen in the walls of bronchi around the bronchial cartilages and mucous glands. In places it could be seen that the material had been deposited concentrically around blood vessels and alveoli and some adjacent masses had become confluent. At some points, the alveoli were fairly well preserved and easily recognizable as such; at other points, near the center of larger masses the alveoli had been so compressed that only a clump

of cells remained. The involved blood vessels were usually of small caliber; in some instances, the walls of these vessels were many times as thick as their lumina. Throughout the sections there were many giant cells which had pink-staining cytoplasm and from five to twenty nuclei.

In sections stained with crystal and methyl violet (Fig. 2), the homogeneous material was stained reddish violet, which is characteristic of amyloid. This reaction was particularly noticeable around blood vessels. The entire tumor was not stained characteristically with methyl violet. In these sections, the deposition of the amyloid in the interalveolar septa was more extensive than was apparent in the sections that had been stained with hematoxylin and eosin. There was a deposition of calcium throughout the tumor mass.

In other sections that were stained with van Gieson's connective tissue stain, the variable staining reaction of the amyloid in different parts of the tumor was evident. The amyloid in the center of the larger masses was stained yellow green while that lying at the periphery of these masses was stained dull red. This dull red color of the amyloid was distinct from the brilliant red of collagen in the sections.

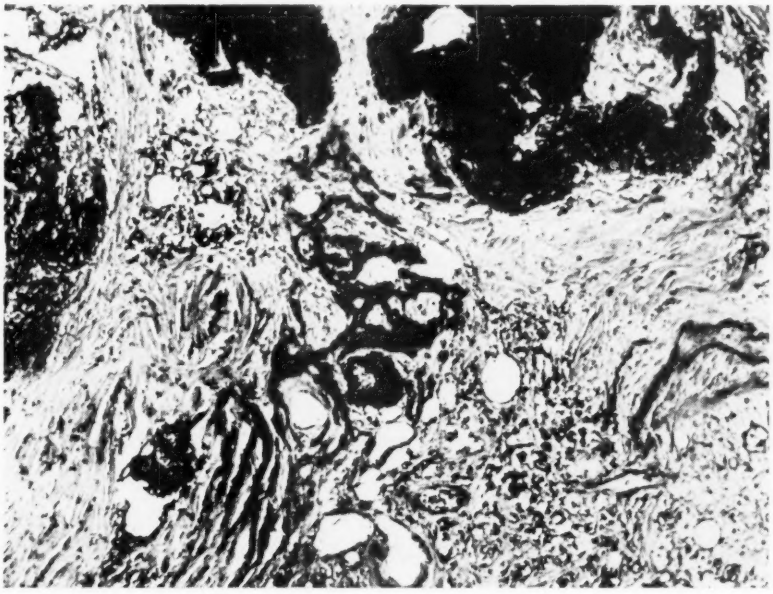

Fig. 2.—The amyloid is deposited in interalveolar septa and in the walls of blood vessels. The dense black material was stained reddish violet with methyl violet. Some of the adjacent masses of amyloid are undergoing coalescence (×100).

The distribution of amyloid was consistent regardless of the staining method that was used. The heaviest and most extensive deposition seemed to have occurred in the alveolar septa and in the walls of blood vessels. The alveoli had been compressed in variable degree and confluence of the masses of amyloid seemed to have formed larger masses which had compressed the bronchus of the middle lobe.

Sections of the lobe beyond the gross limits of the tumor contained some amyloid which usually had infiltrated the interalveolar septa. In general, the histologic appearance of the airless peripheral tissue was that of a chronic pneumonitis with considerable fibrosis.

COMMENT

The case which has been reported has been accepted by us as an example of primary tumor-forming amyloid on the following grounds. There was no history of preceding suppurative disease of the type commonly encountered

in secondary amyloidosis. Although it is impossible to say with certainty that there was not amyloidosis of other mesodermal tissues as seen in cases of diffuse or systemic primary amyloidosis, there was no evidence from the history or physical examination that such involvement existed. The staining reactions with the special stains employed have been accepted as dependable evidence that the tumor was composed of amyloid.

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Surgical Technique

CONGENITAL MACROGLOSSIA

Report of Two Cases

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(From the Department of Surgery, University of California Medical School)

ALTHOUGH a variety of inflammatory and neoplastic processes will increase the size of the tongue in part or in whole,[1] the term macroglossia has come to be reserved for two distinct entities. One is a lymphangiomatous enlargement, and the other a true hypertrophy of the lingual muscle fibers.

Embryologically,[2] the tongue develops in two parts, the buccal and the pharyngeal. These differ in origin, development, structure, and function and are separated by a V-shaped groove, the sulcus terminalis. Our knowledge of the development of the tongue contributes little to our understanding of the etiology of either form of macroglossia. Rigg and Waldapfel,[3] however, have commented on the fissural development of lymphangiomatous growths at the line of union between the anterior and posterior parts of the tongue as lending significant support to the theory of their embryonal origin.

True muscular macroglossia is a congenital hypertrophy of the muscle fibers of the tongue. It may or may not be associated with localized or generalized muscular hypertrophy elsewhere in the body. It is rarely found free from other congenital abnormalities. It is usually associated with cretinism, mongolism, and idiocy. The gross pathologic picture may be one of localized muscular hypertrophy, unilateral enlargement, or a uniform muscular growth of the whole tongue. Bronstein and associates[4] have suggested a practical classification dividing muscular macroglossia into four clinical types. Microscopically there is a definite increase in the diameter of the muscle fibers. Surgery with partial removal has been the treatment of choice in this type (Bassetta,[5] Welzel,[6] and Lengemann[7]). Recently, however, Abelson and associates[8] have questioned the advisability of surgical removal and they have reported a case of spontaneous resolution of true muscular macroglossia.

Lymphangioma is by far the most common cause of macroglossia. This was asserted at an early date by Virchow,[9] Bassetta, and other writers. It has been suggested that a congenital rest which produces new lymphatics, or the congenital absence of afferent lymph vessels, may be an etiologic factor in lymphangiomatous enlargement. The presence of nonpatent lymph vessels, perhaps due to obliteration by subacute infection with resultant obstruction and dilatation of the lymph spaces, has also been proposed as a causative factor.

Lymphangioma may manifest itself as a discrete nodule in the tongue or a diffuse enlargement of the whole organ. The protruding tongue usually becomes dry, fissured, and crusted. Infection occurs resulting in increased fibrosis,

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further obstruction, and progressive enlargement. Microscopically one sees replacement of muscle by lacunae containing scattered red blood cells, constituting a vast lymph vessel tumor. Vesicles on the surface are filled with blood from ruptured adjacent capillaries; the lymph spaces are enlarged and small hemangioma-like areas are produced. Lymphangiomatous macroglossia is frequently

Fig. 1 (Case 1).—Muscular macroglossia. *A* and *B*, Preoperatively, January, 1936; *C*, one month postoperatively; *D*, eleven years later (1947).

associated with lymphangioma of the neck, the so-called cystic hygroma. Lierle[19] reported this association in three cases. The tongue, the floor of the mouth, and the suprahyoid regions may all be involved.

Surgery is indicated in this condition. A wedge-shaped incision is made, preferably by cautery. The tongue is reshaped as close to normal as possible. Postoperatively the maintenance of an adequate airway and the control of oral sepsis are prime considerations. Frequently a secondary resection is necessary. Radiation therapy, although frequently resorted to, offers little help in this

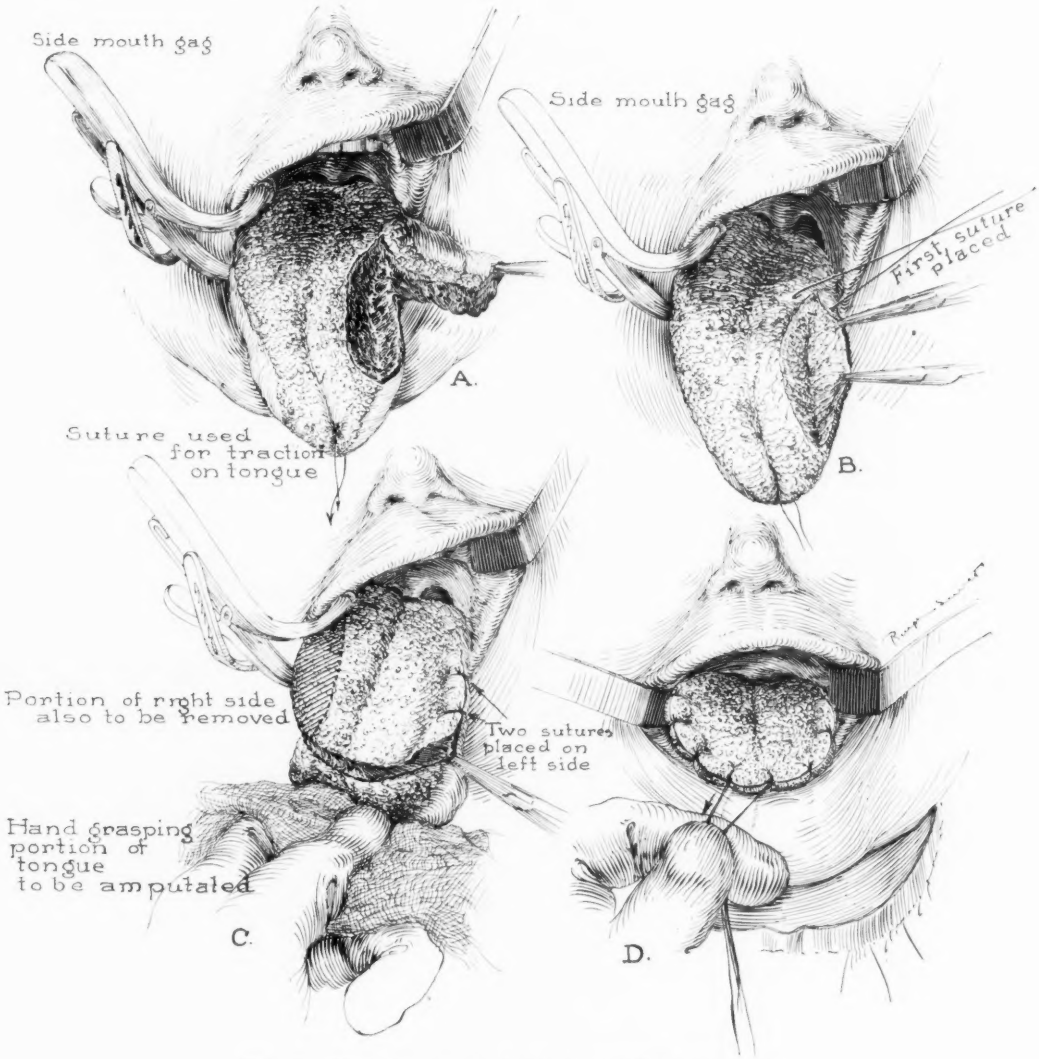


Fig. 2.—Muscular macroglossia; operative procedure.

condition and has not proved as successful as it has for hemangiomatous lesions. Whatever success is attained is usually only temporary and enlargement subsequently recurs.

Biopsy and microscopic examinations are necessary to establish the diagnosis in either form of macroglossia.

CASE REPORTS

We wish to report upon two patients with uniform enlargement of the tongue seen on the surgical service of the University of California Hospital.

CASE 1.—E. A. R., a girl, born five weeks prematurely of a polyhydramniotic mother, had a macroglossia and an umbilical hernia at birth. The hernia was surgically corrected at the time.

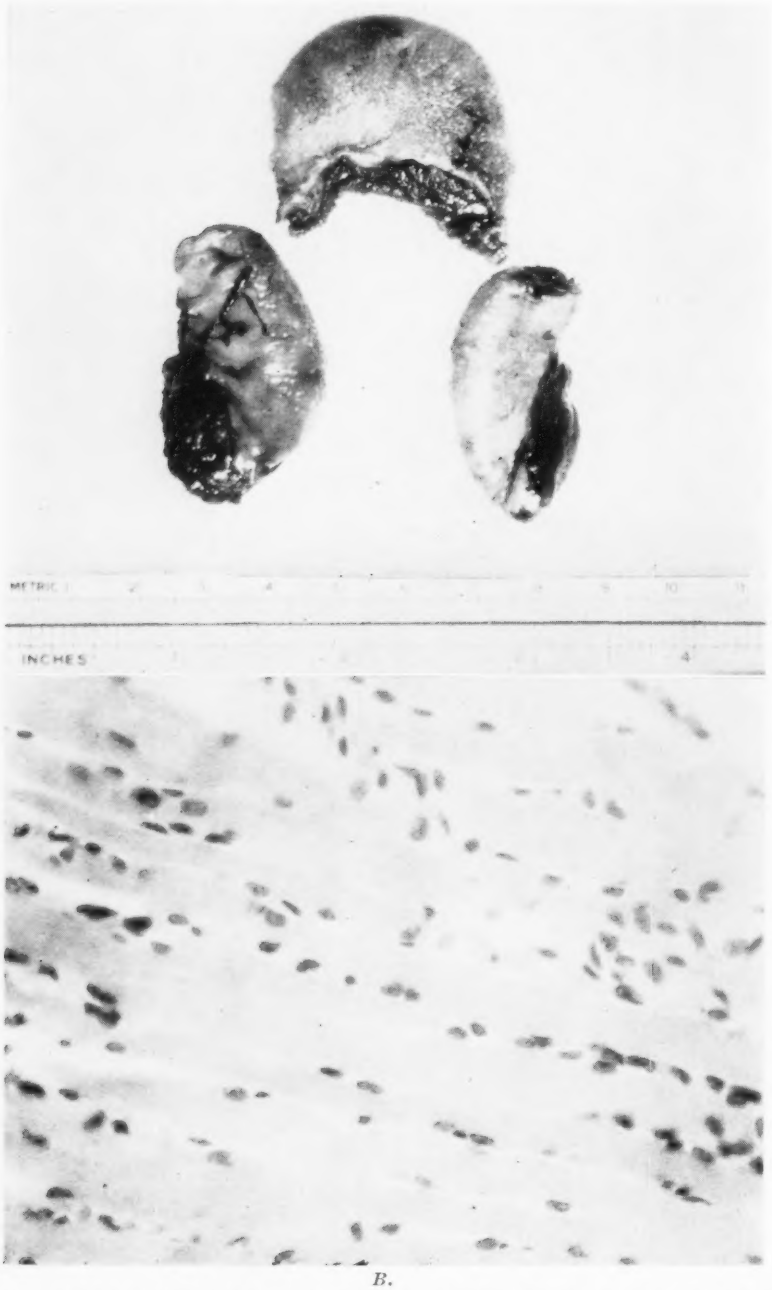


Fig. 3 (Case 1).—Muscular macroglossia. *A*, Surgical specimen, the tip and two lateral wedges of the tongue; *B*, simple muscular hypertrophy with dense interlacing bundles of striated muscle.

The family history was noncontributory. The mother was 36 years old and the father died an accidental death at the same age. One sibling, a 7-year-old boy, was in good health with no abnormalities. One other pregnancy had resulted in a miscarriage six weeks before term.

The child was never breast-fed. She seemed mentally deficient during the first few months but later gave no evidence of maldevelopment. The incisor teeth were present at 6 months of age and all teeth except the upper molars at 27 months. She walked at 18 months and was speaking short sentences at 27 months of age.

On physical examination in January, 1936, when 27 months of age, she weighed 16 kilograms. The tongue was enlarged to four or five times the normal size, completely filled the mouth, and protruded beyond the lips at all times except on swallowing. It did not taper at the tip but was bluntly rounded. The surface showed smooth, uninterrupted

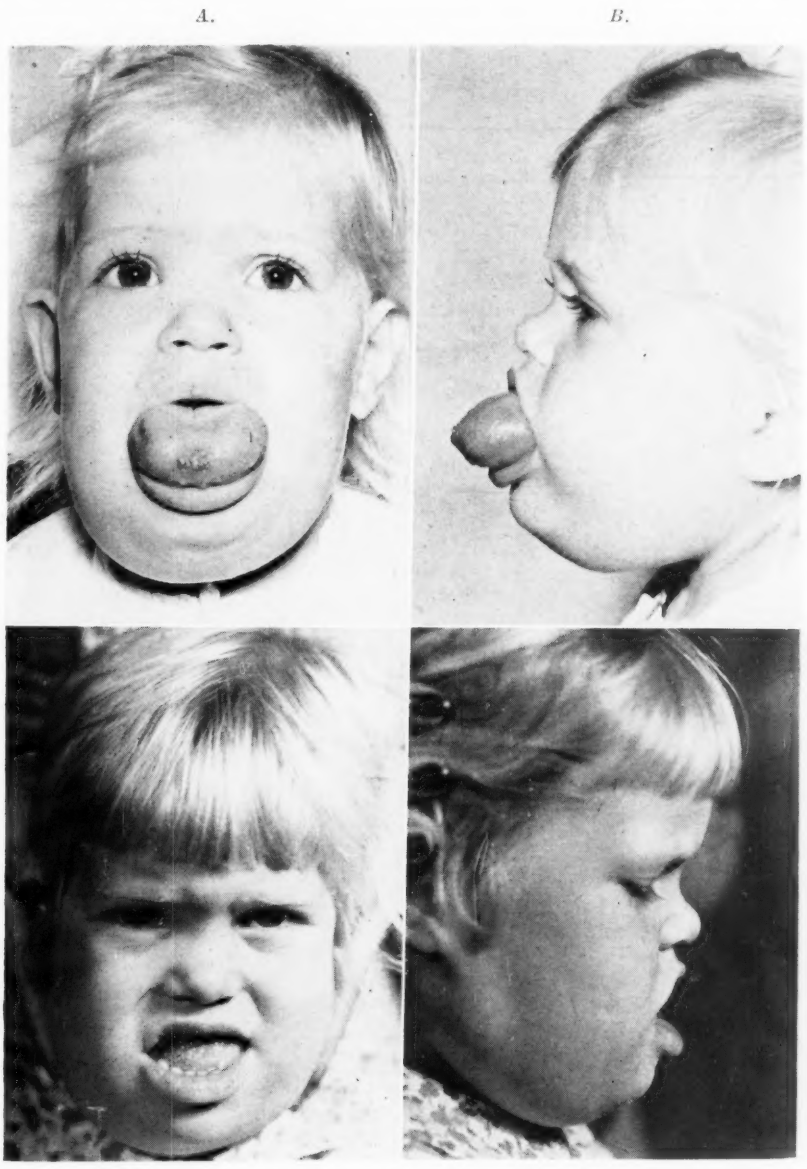
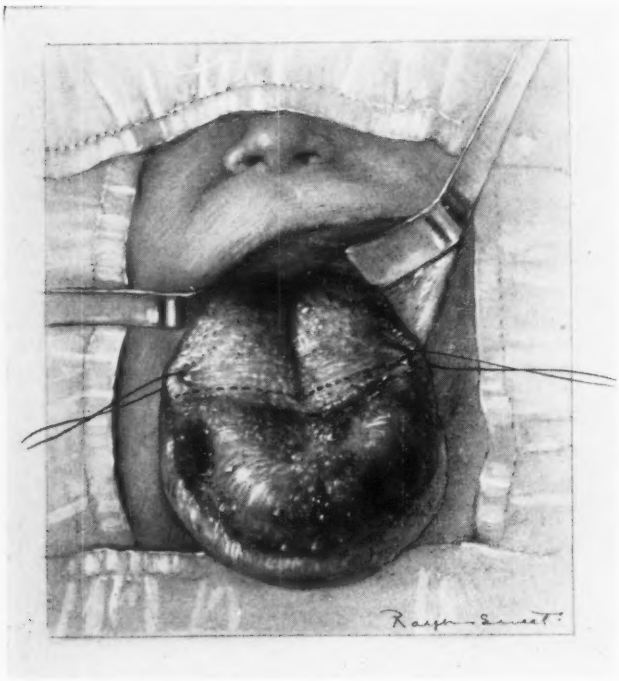


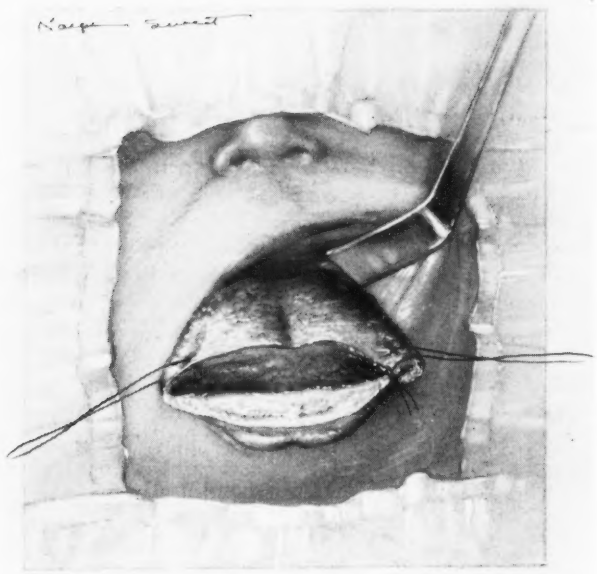
Fig. 4 (Case 2).—Lymphangiomatous macroglossia. *A* and *B*, Preoperatively, October, 1946; *C* and *D*, postoperatively, July, 1947.

A.

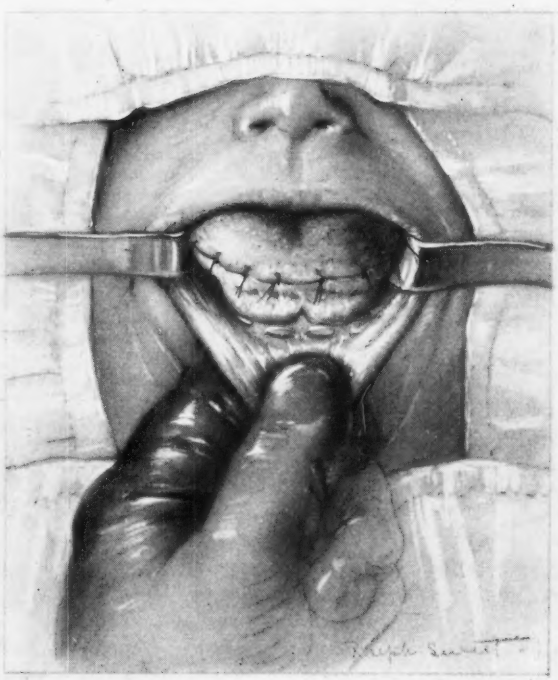


B.

Fig. 5 *A*, *B*, *C*, and *D*.—Lymphangiomatous macroglossia; operative procedure.



C.



D.

Fig. 5, continued.—*(For legend see opposite page.)*

epithelium. The mandible projected forward (prognathism) and x-ray examination showed shortening of the horizontal ramus. The lower incisor teeth were pointing anteriorly from lingual pressure. A small umbilical scar was present. Laboratory studies were not remarkable.

Operation.—Two lateral wedges of lingual tissue were removed, each extending to take a portion of the tip of the tongue. In all, three pieces weighing 19 Gm. were excised (Fig. 3).

Microscopic examination showed simple muscular hypertrophy with densely arranged interlacing bundles of striated muscle. Individual cells were not abnormal. The mucocutaneous membrane was normal.

Subsequent Course.—The child re-entered the hospital in 1937 for incision of an adhesion at the frenulum of the tongue which was restricting its movement. The teeth were straight and the jaw occlusion was improved. In February, 1938, at 4 years of age, the teeth were in normal position. The tongue was much smaller than when she was last seen. She talked well and had difficulty with only a few words, such as "out." Her next visit was not until ten years later (October, 1947) when no sign of defect was noted. Her speech and development had been excellent.

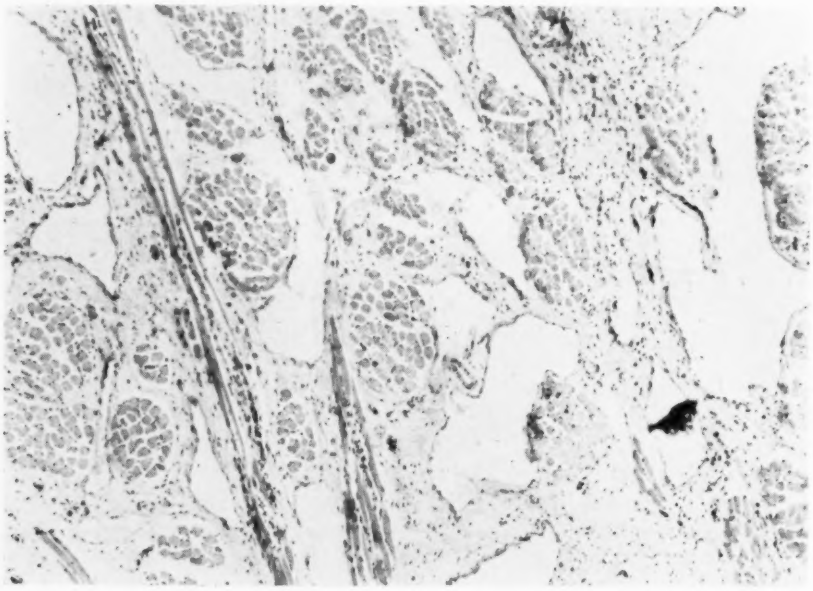


Fig. 6 (Case 2).—Lymphangiomatous macroglossia; widely dilated lymphatics, separate muscle strands, and increased fibrous tissue.

CASE 2.—S. G., a girl, was born in January, 1944, at full term and of normal delivery, with a birth weight of 7 pounds, 1 ounce. At birth the tongue was slightly enlarged with small hemangioma-like areas along the tip. Several cystic swellings the size of pigeon eggs were present in the submandibular areas of the neck. These were transilluminated. The overlying skin was normal. No other abnormal findings were noted.

The family history was irrelevant. The mother and father were both 29 years old and in good health. There were two normal, healthy sisters, 18 months and 4 years old, respectively.

The baby had frequent medical examinations and no change occurred in the tongue or neck swellings until April, 1944. At that time, three months after birth, the tongue began to enlarge rapidly, it increased to three times the normal size, and bleeding occurred from the hemangioma-like areas at the tip.

Development otherwise was normal. She sat alone and had the first tooth at 7 months of age, talked at 12 months, walked at 14 months, and had bladder and bowel control by

2 years of age. She drooled continually, but in spite of the macroglossia was able to take food and talk adequately. Although breathing was sometimes noisy, it was not greatly jeopardized.

Prior to our seeing her, radium therapy was started. In April, 1944, 350 r. were given to each parotid area. There was some regression of the macroglossia, but this was only temporary. Divided doses were administered to the tongue in February, 1946, and altogether a total radium dosage of 7000 mg. hours was delivered to five areas with little effect.

The child was first seen at the University of California Hospital in October, 1946, when physical examination revealed a well-nourished and well-developed girl. There was diffuse total enlargement of the tongue so that it protruded from the mouth, which could not be closed. The anterior portion was fissured and crusted. The fauces were covered with crustings. An even, doughlike enlargement of the neck tissues in the suprahyoid regions gave a heavy jowl to the little girl. Multiple cystic swellings were palpable here on the right. The lower incisor teeth projected dramatically forward from the pressure of the bulky tongue upon the dental arch. In spite of this disability she could speak, and was intelligent and cooperative. Findings in the remainder of the physical examination were negative. No other congenital abnormalities were found. An x-ray film of the chest was normal. Laboratory studies were not unusual. There was no evidence of micrognathia and roentgenograms of the temporomandibular joints showed no displacement.

Operation.—Several large, cystic polyps were seen arising from the base of the tongue and hanging down toward the epiglottis, obstructing the airway. These were removed. The anterior portion of the huge tongue was resected in an elliptical fashion by cautery, and the tongue was reshaped as well as possible (Fig. 5).

Microscopic examination revealed marked lymphangiectasis and fibrosis. The lymphatics were widely dilated, separating the muscle strands and increased fibrous tissue. There was mild lymphocytic and plasma cell infiltration with acanthosis and metaplastic keratosis of the epithelial layers. The pharyngeal cysts were made up of extensively dilated, proliferating lymphatics.

Subsequent Course.—The child was last seen in October, 1947, at 3 years of age, when there was marked improvement in appearance. The mouth was closed. The tongue had shrunk greatly but was still edematous. The cystic masses in the neck were somewhat firmer. Further treatment is not contemplated until maximum improvement has occurred.

SUMMARY

A brief discussion of congenital macroglossia is presented.

Two cases, one of muscular macroglossia, the other of lymphangiomatous macroglossia associated with cystic hygroma of the neck, are reported.

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Recent Advances in Surgery

Conducted by Alfred Blalock, M.D.

THE RELATIONSHIP OF BONE TRAUMA TO THE DEVELOPMENT OF ACUTE GASTRODUODENAL LESIONS IN EXPERIMENTAL ANIMALS AND IN MAN

With Particular Reference to the Role of Fat Emboli

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HISTORICAL

THE occurrence of fat embolism following trauma in man was first recognized in 1862 by Zenker[1] who described a case of fat embolism of the pulmonary capillaries in a laborer who died following a crush injury with multiple fractures of the ribs. That fat embolism in the lung and brain are common occurrences in patients dying early after fracture of long bones is well known.[2, 3] Warthin,[4] in an extensive review of the literature in 1913, stated that, "it is highly probable that in every case of amputation or fracture of the long bones some fat is set free from the ruptured fat-cells and . . . enters the blood stream to cause fat-embolism in the pulmonary capillaries, or, passing the lungs, in the capillaries of some other organ. . . The gravity of the condition will depend upon the anatomical importance of the capillaries blocked by the fat-emboli." He reported, in addition, twelve cases of fat embolism, out of a relatively small post-mortem service of 560 autopsies, nine of the twelve following fracture of the long bones. Of the fracture cases terminating fatally, post mortem examination in all showed a marked fatty embolism as the cause of death.

Warthin stated that the mechanism of fat embolism following fracture is a release of liquid fat from the marrow of the fracture site which gains entrance into the vascular system by virtue of increased tension at the site of injury forcing the fat into the open veins of the bone. In addition, there is entrance of free fat into the lymphatics; this occurs later than the direct entrance of fat into the circulation. The fat droplets enter the thoracic duct and then pass through the venous circulation into the lungs, constituting a second supply of fat to reach the lungs.

Fat embolism of clinical importance occurs most commonly following fractures of the bones containing fatty marrow; less frequently it is caused by injury to adipose tissue. Osteoporotic bones in old people, or in young individuals who possess atrophic bones from non-use, are especially likely to

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yield, on injury, a sufficient amount of fat to cause lipemia and embolism. Fractures of the tibia and femur are the most frequent causes of fat embolism. Scriba[5] calculated the amount of fat present in the average adult femur to be 71 Gm. In studies relating to experimental fat embolism he calculated that the femur of a dog weighing 17 kilograms contains on the average 12.7 Gm. of fat, while the femur of a rabbit weighing 2 kilograms contains an average of 1.3 Gm. of fat.

Of the numerous accounts of fat embolism of the lung, brain, and kidney following fracture, only occasional reference is made in the literature to the occurrence of embolic phenomena in the capillaries of the gastrointestinal tract. Scriba,[5] in 1879, noted fatty emboli with capillary hemorrhage in the mucosa of the stomach and intestine. LeCount and Gauss[3] noted fat emboli in the vessels of the gastric mucosa in some of their fourteen cases of fat embolism associated with fractures at autopsy. Warthin[4] stated that there is not a single organ or tissue in the body that does not get some fat in its capillaries during a fatty embolism and he has found emboli of fat to occur in the capillaries of the stomach and intestine.

Furthermore, the only allusion to the occurrence of gastrointestinal erosion and/or ulcer following fracture, other than that made by one of us (O.H.W.[6b]) in 1945, is to be found in a discussion of a paper by Sternberg in 1907. Schridde,[7] in this discussion, stated that he had twice observed fat embolism at post-mortem in the submucosal gastric arteries accompanying fracture. In one patient, a 70-year-old man, there were numerous erosions and twenty superficial ulcers. The patient died of coma which had persisted following the fracture. Schmorl,[8] in a six-line discussion at the same meeting of the German Pathological Society, stated that he too had observed punctate hemorrhages in the gastric mucosa due to fat embolism following fractures and severe bodily contusions. Vale and Cameron,[9] in a paper concerning the occurrence of gastric and duodenal perforation during hospital treatment, reported a case of a 55-year-old man who, being struck by an automobile, sustained a fracture of the right clavicle and a compound fracture of the right leg. Twenty-one days after injury and treatment of the fractures, and while on a regimen of bed rest and a soft diet, the patient developed a perforated duodenal ulcer which was surgically closed. They stated that "trauma sustained at the time of injury may be mentioned as a possible causative factor."

Gastrointestinal bleeding on a psychic or emotional basis following minor surgical procedures in four cases was reported by Brooke.[10] Herbut[11] observed five patients who developed acute peptic ulcers following distant operations. He stated that the causes of the ulcers were not apparent.

Experimentally, Magendie,[12] during the years 1821 to 1836, before the occurrence of pathologic fat embolism in man was known, performed many experiments upon animals to determine the effects of the injection of oil into the circulating blood, and discovered that the fluid fat would not pass the smaller vessels, but blocked them mechanically. Lower,[13] in 1669, had injected large amounts of milk intravenously into dogs. Scriba[5] (1879) pointed out that a drop of fat could pass through the lungs without difficulty. Lehman and

Moore[14] in 1927 presented experimental evidence suggesting a nontraumatic origin of fat embolism—the source of fat being the ultramicroscopic emulsion of fat in the normal blood plasma which may form fat droplets of emboli due to physical or chemical alterations in the blood. Virchow[15] in 1862 showed that the experimental injection of minutely emulsified fat was not followed by embolism. He was one of the first to foster the theory of vascular blocking in the genesis of peptic ulcer—a deduction which Virchow made from observing the funnel-shaped character of many ulcers.

PRESENT STUDY

Experimental studies concerning the relationship of fracture of long bones to gastroduodenal pathology have been reported in abstract form from this clinic previously.[16-19] The studies have been enlarged upon. This presentation embodies a series of studies concerning the relative incidence of acute gastroduodenal ulcer and/or erosions complicating fractures and amputations of long bones in patients dying early after fracture or amputation and submitted to necropsy, as well as two patients who recovered following fracture. In addition, experimental evidence is presented concerning the occurrence of similar gastroduodenal lesions in animals subjected to operative fracture or intravenous administration of nonemulsified fat.

A. STUDY OF THE INCIDENCE OF GASTRODUODENAL ULCER AND/OR EROSION COMPLICATING FRACTURE OF LONG BONES IN MAN

The observation of a few cases of hematemesis from erosion or ulcer complicating fracture of bones in man, reported in 1945,[6a] prompted a review of the records from the files of the Department of Pathology of the University of Minnesota concerning fractures in patients coming to autopsy. Over a period of time extending from 1920 to August, 1947, there were 1,432 autopsies performed on individuals who died following fractures of bones, excluding skull fractures. The etiologic factors involved in the occurrence of peptic ulcer in head trauma may be complex, particularly, as Cushing[20] has suggested, if the diencephalon is involved. Also, those cases in which there was a question of post-mortem autolysis of tissue or evidence of chronicity of the ulcers, clinically or pathologically, are not included in the study.

In a series of 1000 consecutive autopsies of patients dying of all causes, it was noted by one of us (F.B.M.) that forty patients demonstrated gastroduodenal ulceration, eight of whom died of peptic ulcer per se and its complications. Thus, thirty-two patients presented coincidental gastroduodenal ulceration (acute and chronic, but excluding healed scars of ulcers); however, in six of these cases it was not possible to rule out entirely changes due to autolysis and post-mortem digestion. The incidence of coincidental acute and chronic ulcers, then, is between 2.6 and 3.2 per cent among routine autopsies.

Twenty-seven cases, demonstrating at autopsy acute or subacute ulceration or erosion of the stomach and/or duodenum following fracture, are listed in Table I. In addition, two cases with recovery are appended. It is to be noted in this tabulation that 23 of the 27 cases presented at autopsy definite ulceration (eight gastric, fourteen duodenal, and one both gastric and duodenal).

In the four remaining cases definite erosions and petechial bleeding points were noted in the stomach and duodenum. The age of the patients ranged from 17 to 93 years, the majority being about 55. The time of death after fracture varied from one to eighty-three days, death occurring within three weeks from the time of fracture in all but five cases. Hemorrhage from the gastrointestinal tract, recognized clinically and recorded as hematemesis or melena, was observed in twelve of the twenty-nine cases tabulated; in five additional instances autopsy revealed evidence of bleeding not recognized clinically. Ulcer therapy was instituted in seven cases diagnosed clinically; two of these patients recovered completely. One patient (L. W., Hospital No. 702724), a 36-year-old man, having sustained multiple fresh fractures in an automobile accident, was admitted to the University Hospital on Dec. 10, 1940; fat was demonstrated in

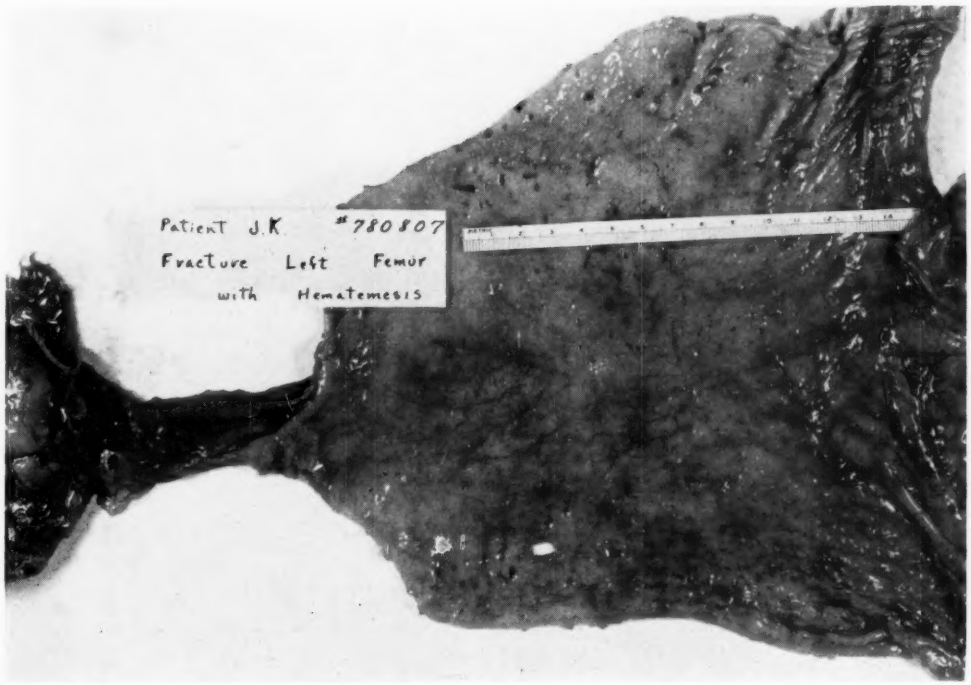

Fig. 1.—Stomach with minute gastric ulcers and bleeding points from patient, J. K. (Hospital No. 780807), aged 93 years (see Table I, Case 26), who entered the University Hospital on Aug. 3, 1947, with a fresh fracture of the left femur. On the third hospital day a massive hematemesis occurred and a clinical diagnosis of gastric bleeding due to fat embolism was made. The hemorrhage persisted despite administration of anti-acids and blood transfusions and the patient died on the eighth hospital day.

the urine of the patient the day following admission, but no abnormal lipemia was observed. He suffered one episode of dyspnea. On the twenty-second hospital day hematemesis occurred, followed by melena, which continued for one week, necessitating blood transfusions. The prothrombin time and vitamin C level in the blood were normal. The patient eventually made a satisfactory recovery and was dismissed to his physician. There had been no antecedent story of ulcer or bleeding. Another patient (E. N., Hospital No. 718858), a 68-year-old man, was admitted to the University Hospital on March 27, 1942; melena occurred thirty-five days after a fresh fracture of the neck of the right

TABLE I. SUMMARY OF CASES PRESENTING ACUTE GASTRODUODENAL ULCER AND/OR EROSIONS IN PATIENTS WHO DIED EARLY AFTER FRACTURES OF LONG BONES, TOGETHER WITH TWO CASES WITH RECOVERY

NO.	PATIENT	AGE (YR.)	SEX	FRACTURE SITE	CLINICAL EVIDENCE OF GI HEMORRHAGE (+ OR 0)	TIME INTERVAL BETWEEN FRACTURE AND DEATH (DAYS)	GASTROINTESTINAL FINDINGS AT AUTOPSY	REMARKS
1	E. W.	56	F	Left femur	+	46	Multiple acute gastric ulcers 1 cm., no induration	Hematemesis the following day after manipulation and cast of fracture
2	E. H.	53	F	Rt. tibia	0	14	Posterior duodenal ulcer—4 mm., punched-out; no induration	Manipulation and cast of fracture
3	J. McD.	73	M	Bilateral tibia and fibula, and pelvis	0	2	Posterior duodenal ulcer, 6 cm.	Marked cerebral fat embolism at autopsy
4	U. C.	24	M	Ribs and pelvis	0	1½	Anterior duodenal ulcer 8 mm., acute	Acute alcoholism
5	J. W.	55	F	Bilateral tibia, fibula, rt. radius, left humerus and pelvis	0	1	Antral erosions	Immediate cause of death unknown
6	C. S.	60	M	Rt. femur, comminuted	0	83	Subacute prepyloric ulcer, 5 cm., hemorrhagic base; slightly rolled edges	Died 2 days after manipulation of fracture; cerebral fat embolism at autopsy
7	J. P.	69	M	Left ribs 3rd to 7th	0	7	2 prepyloric ulcers, 2 mm.; 2 duodenal ulcers, 2 cm.; sl. induration, hemorrhagic	Syphilitic history
8	J. M.	67	M	Rt. tibia and fibula, and pelvis	+	6	3 hemorrhagic gastric ulcers 5-7 mm., multiple bleeding points, entire GI tract contained old blood	Hematemeses 3rd and 6th day with exsanguination and death

9	K. D.	83	F	Left femur, neck	0	44	Minute duodenal ulcers, small intestine filled with blood	Arteriosclerosis with hypertension
10	A. S.	60	M	Rt. tibia and fibula compound and comminuted	0	4	Gastric ulcer, 2 cm.	Amputation rt. leg on 2nd day; died gas bacillus infection
11	A. O.	42	M	2nd Lumbar vertebra	0	7	2 duodenal ulcers, 1 cm.	Intoxicated at time of fracture
12	M. McD.	68	M	Left femur, intertrochanteric, comminuted	+	3	Multiple hemorrhagic gastric erosions, 2-5 mm.	Hematemesis 3rd day; died of bronchopneumonia
13	G. A.	69	M	Left ribs 9, 10, 11	+	16	Perforating duodenal ulcer 32 × 22 mm., no induration; blood in intestinal tract	Admitted to hospital 14th day with an acute abdomen, melena, anemia, dyspnea
14	R. B.	63	M	Rt. femur head, fracture-dislocation	0	11	Several prepyloric ulcers, 4-6 mm.	Paralytic ileus
15	R. L.	79	M	Rt. humerus	0	19	Posterior duodenal ulcer, 1.5 cm., no induration	Died coronary occlusion
16	K. S.	82	F	Left femur, subtrochanteric	+	14	Perforating posterior duodenal ulcer 1.5 × 2.5 cm.; soft margins antral, gastritis	Hematemesis 10th day with subsequent diagnosis of ulcer and institution of ulcer therapy; died of pneumonia
17	M. L.	17	M	Rt. femur, compound	+	27	2 gastric hemorrhagic erosions and multiple bleeding points	Hematemesis 20th day; skeletal traction lower femur
18	E. L.	91	M	Left femur, intracapsular	0	16	Duodenal ulcer, rounded edges	Died of pneumonia
19	C. J.	70	F	Rt. femur, intracapsular	0	33	Duodenal ulcer 0.5 cm., no induration	Fixation of femur with Smith-Petersen nail

TABLE I—CONT'D

NO.	PATIENT	AGE (YR.)	SEX	FRACTURE SITE	CLINICAL EVIDENCE OF GI HEMORRHAGE (+ OR 0)	TIME INTERVAL BETWEEN FRACTURE AND DEATH (DAYS)	GASTROINTESTINAL FINDINGS AT AUTOPSY	REMARKS
20	P. P.	91	F	Rt. femur, intertrochanteric	0	26	2 posterior duodenal ulcers, bleeding 2.5 cm. and 1 cm. rounded edges; old blood in colon	Cardiac failure; died of pulmonary embolism
21	E. G.	45	M	Bilateral clavicles	+	9	Gastric ulcer, 1.5 cm. superficial	Large hematemesis 4th day; numerous fat particles in serum 7-25 micra in size, urine negative; clinical diagnosis fat embolism to stomach, brain, kidneys, and lungs
22	J. A.	83	M	Rt. femur, rt. tibia, and fibula	0	24	2 duodenal ulcers, 1 cm. diameter; slight induration	Hypertension
23	A. H.	65	F	Rt. femur, intertrochanteric	+	12	Superficial elongated ulcer, postduodenal 2.1 cm. with 2 bleeding points at base	Hypertension, diabetes, massive hematemesis 9th day which persisted; fat embolism at autopsy
24	E. G.	72		Rt. ribs	0	46	Active duodenal ulcer, 1.5 cm.	
25	E. C.	82		Left femur	0	3	Hemorrhagic erosions (2 cm.) in gastric mucosa	Cholecystitis and cholangitis
26	J. K.	93	M	Left femur	+	8	Multiple minute gastric ulcerations and bleeding points	Hematemesis on 3rd day, coffee ground; 58° free acid to histamine, treated for ulcer
27	J. B.	24	M	Rt. femur, rt. tibia, and fibula	+	3	3 hemorrhagic gastric ulcers in cardia, acute without induration	Hematemesis in 24 hr., diagnosed and treated for ulcer with amphogel drip, microscopic fat embolism

28	L. W.	36	M	Rt. femur, rt. ischium, left transverse processes of 3rd and 4th lumbar vertebrae	+	Recovery		Hematemesis on 22nd day, repeated, and followed by melena, diagnosed as acute bleeding ulcer and treated with frequent feedings and multiple transfusions; dyspnea, fat demonstrated in urine; plaster immobilization of fracture, barium x-ray studies, unsatisfactory questionable duodenal ulcer
29	E. N.	68	M	Rt. femur, mid-cervical	+	Recovery		Melena on 35th day with marked fall in hemoglobin, epigastric pain relieved by food, gastroenterostomy 18 yr. previously with only mild infrequent distress in the interval, barium x-ray studies at 60 days demonstrated large stomal ulcer, 2 cm.; repeat study 3 mo. later showed healing ulcer, 18° free acid in fasting state
Cases following amputation:								
30	D. W.	75	M	Low thigh amputation, ice anesthesia	0	1	Acute gastric ulcer 1 cm. on lesser curvature	Arteriosclerotic gangrene of rt. foot; coronary sclerosis, diabetes mellitis
31	J. B.	60	F	Rt. supracondylar amputation	0	73	Multiple gastric ulcers, 3-10 mm., slightly elevated margin	Arteriosclerotic gangrene rt. foot, arteriosclerotic heart disease with terminal failure

femur. Associated with the onset of melena, a sudden and marked drop in hemoglobin occurred, for which blood transfusions were given. The stools were consistently positive for blood for two weeks. Gastric aspiration without histamine stimulation revealed 18 degrees free acidity and 34 degrees total acidity. The patient had undergone gastrojejunostomy elsewhere eighteen years previously for duodenal ulcer. He had experienced only mild infrequent epi-gastric distress in the intervening years, but this was the first hemorrhage since operation. X-ray examination of the gastro-intestinal tract with a barium meal sixty days after the fracture revealed a large stomal ulcer 2 cm. in diameter. The patient did well on an ulcer regime and was dismissed from the hospital on crutches. X-ray examination three months later demonstrated healing of the stomal ulcer, no crater being made out. There has been no recurrence of ulcer symptoms since the fracture. It was felt that this episode represented an acute ulceration following fracture.

In reviewing the records of the University Hospital from 1920 to 1946, seventeen patients who died early after surgical amputation of the thigh were submitted to necropsy. One patient (D. W., Hospital No. 737507, Table I), a 75-year-old man, underwent a low thigh amputation with ice anesthesia for arteriosclerotic gangrene of the right foot on Nov. 18, 1843. He died suddenly the following day. Post-mortem examination revealed an acute gastric ulcer 1 cm. in diameter on the lesser curvature. There was no history of contributory gastrointestinal symptoms. Studies for fat embolism were not done. Another patient (J. B.), a 60-year-old woman, whose records were obtained from the department of pathology files, died seventy-three days after a right supracondylar amputation for arteriosclerotic gangrene of the right foot. Post-mortem examination revealed multiple gastric ulcers 3 to 10 mm. in diameter with slightly elevated margins. Similarly, there was no history of gastrointestinal disease. In addition, it is to be noted that one patient (Case 10, Table I) underwent amputation for compound fractures of the right tibia and fibula.

In response to an inquiry addressed to fifty American orthopedic surgeons concerning the occurrence of spontaneous hematemesis as a sequel to fractures of long bones or after manipulative procedures upon bones or joints, forty-two replies were received. One surgeon stated that he had observed a patient in whom sudden hematemesis and melena occurred four days after fracture of the left femur. The patient had undergone surgical closure of a perforated duodenal ulcer sixteen years previously and had no gastrointestinal complaints in the intervening years. The patient recovered under an ulcer regime and blood transfusions, and had no further difficulty. Another surgeon disclosed having seen a patient in whom a severe and spontaneous gastric hemorrhage followed a laminectomy for protruded intervertebral disc. The patient later underwent a subtotal gastric resection for ulcer. Another surgeon noted three cases of fracture in which a subsequent loss of blood was found to have as its source the gastrointestinal tract inasmuch as blood was found in the stools of these patients. Two surgeons each reported having observed hematemesis once after the manipulation of a stiff joint or contracture under anesthesia. No others reported observing ulcer or hematemesis in patients not previously having ulcer.

B. THE EXPERIMENTAL PRODUCTION OF GASTRODUODENAL ULCERATION AND/OR EROSION IN LABORATORY ANIMALS BY FRACTURE OR CURETTEMENT OF BONE MARROW (WITH REFERENCE TO THE ULCER DIATHESIS)

The observations made in the clinical cases reported in the foregoing suggested the necessity of determining whether ulcer could be produced in experimental animals by fracture of the long bones. The occurrence of spontaneous gastroduodenal ulceration in dogs is unknown. Accordingly, ninety-one dogs were subjected to a drill hole through both cortices of the humerus, with and without curettement of the bone marrow, or fracture. Normal adult dogs were employed and the operative procedure was carried out under intravenous sodium pentobarbital anesthesia with sterile technique. The drill hole was made with a power-driven (electric) drill measuring 1/4 inch. The diet of the experimental dogs was varied in different series. All dogs were sacrificed with an overdose of sodium pentobarbital twenty-one days after the operative procedure and the gastrointestinal tract was examined in each instance. Forty-five of the ninety-one dogs (49 per cent) subjected to operative fracture of the humerous demonstrated positive gastroduodenal pathology when sacrificed. Ten showed ulcer and/or erosion of the stomach or duodenum (11 per cent). In one instance, a perforated duodenal ulcer was observed. The remainder of the forty-five dogs presented a mild to severe gastritis and/or duodenitis, with frequent evidence of hemorrhage from petechial bleeding points. The animals were free of any associated illness and all were sacrificed. The varied diets were found to be of no significance in the incidence of gastrointestinal pathology in the different series of dogs.

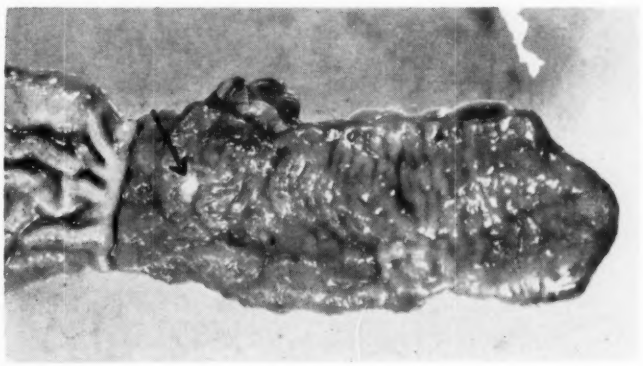

Fig. 2.—Antrum and duodenum from Dog 22 subjected to curettage of the bone marrow of the right humerus illustrating perforated duodenal ulcer. No administration of histamine.

A series of six guinea pigs, weighing 280 to 445 grams, was subjected to fracture of a femur. All fractures were produced by direct trauma under ether anesthesia. Two of the animals received repeated fractures of other long bones. No restriction of food or water intake was made and the animals were sacrificed from ten to sixty-one days following fracture, at which time the gastrointestinal tract was immediately examined. One of the six guinea pigs developed a gastric ulcer. An equal number of cats was treated in a similar fashion; no gastrointestinal pathology was observed.

Having demonstrated that ulcer and/or erosion of the stomach and duodenum in animals may follow the experimental production of fracture or curettage of the bone marrow, it remained to be shown whether experimental fractures in animals would abet the ulcer diathesis. Ulcers of the stomach and duodenum have been produced in dogs quite consistently in this laboratory over an eight-year period, employing daily intramuscular injections of histamine-in-beeswax mixture, thus inciting a maximal gastric secretory response over a period of twenty-four hours after each injection. It was shown by Hay and associates[21] that in forty days ulcers may be produced regularly in dogs by this method. The average appearance time of the ulcers was twenty-three days. In another series of fourteen control dogs to which 30 mg. of histamine-in-beeswax were administered daily, killed from four to fourteen days after commencement of the administration of histamine, ulcer was observed in one dog, after seven doses of histamine. Over an eight-year interval during which time histamine-in-beeswax was given to a large number of dogs, ulcer was observed twice at four days following the daily administration of 30 mg. of histamine implanted in beeswax. It was also shown[21] that bona fide ulcers in rabbits cannot be produced with histamine alone. Any condition, therefore, which may increase the susceptibility of the gastric or duodenal mucosa to the erosive action of gastric juice, or any circumstance which hastens the development of the histamine-induced ulcer as measured by a reduction in time of development to within six days after commencement of daily injections, is considered an abetting influence of the ulcer diathesis. Similarly, any condition which favors the development of a gastric or duodenal ulcer in rabbits when histamine-in-beeswax administration is employed may be considered to abet the ulcer diathesis.

Accordingly, a study was carried out utilizing twenty-three dogs and thirteen rabbits. Eighteen of the twenty-three dogs were subjected to a drill hole through both cortices of the right humerus with curettage of the bone marrow with a pliable wire under sodium pentobarbital anesthesia (15 mg. per pound body weight intravenously). The operative procedures were carried out under sterile precautions. Administration of daily intramuscular injections of histamine-in-beeswax mixture (30 mg. base) prepared after the method of Code and Varco[22] was begun the day of operation. Five dogs, serving as controls, were anesthetized but were not subjected to an operative procedure, and received daily injections of histamine-in-beeswax. All animals were fed each morning a standard diet of table scraps and dog kibbles, the food pans being removed each evening. Three dogs died four and five days following operation. The remaining dogs were sacrificed in six days or less, and sections of the stomach, duodenum, brain, lung, and kidney were obtained for microscopic study. One additional dog sustained spontaneous fractures of both forelegs when it jumped from its cage on an upper tier of cages to the floor, a distance of about seven feet. This dog was then given six daily injections of histamine-in-beeswax and sacrificed at the end of that time.

Thirteen rabbits were subjected to fracture of the humerus under intravenous sodium pentothal anesthesia and received, in addition, daily intra-

muscular administration of histamine-in-beeswax (15 mg. base). Some also received curettage of the bone marrow at the time of operative fracture. No dietary restrictions were imposed and all animals were sacrificed from six to thirty-one days after fracture. Sections of the stomach, duodenum, brain, lung, and kidney were obtained for microscopic study.

As is noted in Table II, fourteen of the eighteen dogs subjected to a drill hole of the humerus, with curettage of the bone marrow accompanied by histamine-in-beeswax administration, demonstrated abnormal gastroduodenal findings in six days or less. Of the fourteen dogs, nine showed definitive gastric or duodenal ulcers (one perforated and one perforating) and two showed erosions of the mucous membrane. Definite bleeding points and hemorrhagic petechiae were noted in the stomach and duodenum of nine dogs. The one dog which sustained spontaneous fracture of both forelegs and was given six daily injections of histamine-in-beeswax presented a large gastric ulcer when sacrificed in six days. Five control dogs subjected to anesthesia but to no operative procedure presented no pathologic gastrointestinal findings when sacrificed after five and six daily injections of histamine-in-beeswax mixture.

Fig. 3.—Duodenal ulcer and antral bleeding points from Dog 618 (see Table II) subjected to curettage of the bone marrow of the right humerus in addition to six daily intramuscular injections of histamine-in-beeswax.

One of the thirteen rabbits subjected to fracture of the humerus accompanied by histamine-in-beeswax administration showed a gastric ulcer when sacrificed in six days.

Microscopic study of the tissues obtained from these animals will be discussed later in this presentation.

C. STUDIES CONCERNING GASTRIC SECRETION IN CLINICAL CASES OF FRESH FRACTURE OF LONG BONES AND AFTER OPERATIVE FRACTURE IN EXPERIMENTAL ANIMALS

1. *Studies of Gastric Secretion in Clinical Cases of Fresh Fracture.*—A review of the data cited in Table I concerning the occurrence of gastroduodenal

TABLE II. OCCURRENCE OF GASTRODUODENAL ULCER AND/OR EROSIONS IN DOGS SUBJECTED TO DRILL HOLE OF THE RIGHT HUMERUS WITH CURETTAGE OF THE BONE MARROW, ACCOMPANIED BY DAILY ADMINISTRATION OF HISTAMINE-IN-BEESWAX MIXTURE

DOG NO.	WT. (IN LB.)	OPERATIVE PROCEDURE	DAILY DOSE OF HISTAMINE (MG.)	NO. OF INJ.	RESULTS	REMARKS
586	48	D. H.*	30	4	2 duodenal ulcers, one perforated; gastric bleeding points	Died 4th day, peritonitis
582	37	D. H.	30	5	Duodenal erosion; gastric bleeding points	Died 5th day, pneumonia
603	29	D. H.	30	4	Essentially negative stomach and duodenum	Sacrificed 4th day
604	30	D. H.	30	4	Essentially negative stomach and duodenum	Sacrificed 4th day
605	32	D. H.	30	6	Perforated duodenal ulcer; gastric bleeding points	Sacrificed 6th day
606	31	D. H.	30	4	Essentially negative stomach and duodenum	Sacrificed 4th day
607	35	D. H.	30	5	Duodenal ulcer; hemorrhagic gastritis	Died 5th day, exsanguination
608	28	D. H.	30	5	Early duodenal ulcer; antral bleeding points	Sacrificed 5th day
609	18	D. H.	30	6	Negative stomach and duodenum	Sacrificed 6th day
610	24	D. H.	30	5	Duodenitis; antral bleeding points	Sacrificed 5th day
611	19	D. H.	30	6	Duodenal ulcer	Sacrificed 6th day
612	23	D. H.	30	1	Hemorrhagic duodenitis	Sacrificed 24 hours
613	30	D. H.	30	5	Bleeding antral erosions	Sacrificed 5th day
614	36	D. H.	30	5	Antral bleeding points	Sacrificed 5th day
615	37	D. H.	30	5	Petechial gastric ulcer and bleeding points	Sacrificed 5th day
616	33	D. H.	30	6	Early duodenal ulcer	Sacrificed 6th day
617	28	D. H.	30	6	Multiple gastric ulcers	Sacrificed 6th day
618	34	D. H.	30	6	Duodenal ulcer and gastric bleeding points	Sacrificed 6th day
43	24	No operation; spontaneous accidental fracture of both forelegs	30	6	Large gastric ulcer	Sacrificed 6th day
		Controls (anesthesia, histamine, but no curettage of bone marrow)				
1	32	0	30	5	No ulcer, erosion, or bleeding points	Sacrificed 5th day
2	26	0	30	5	No ulcer, erosion, or bleeding points	Sacrificed 5th day
3	29	0	30	5	No ulcer, erosion, or bleeding points	Sacrificed 5th day
4	19	0	30	6	No ulcer, erosion, or bleeding points	Sacrificed 6th day
5	30	0	30	6	No ulcer, erosion, or bleeding points	Sacrificed 6th day

*Drill hole with curettage of bone marrow.

ulcer in patients with fracture of the long bones suggested the possibility of stimulation of gastric secretion due to histamine liberation from the site of trauma. Studies of gastric secretion were carried out on ten consecutive patients admitted to the University Hospitals with fresh fractures of bone. Gastric secretions were obtained for analyses by gastric intubation of these patients

Fig. 4.—Gastric ulcer and multiple petechial ulcers from Dog 617 (see Table II) subjected to curettage of the bone marrow of the right humerus in addition to six daily intramuscular injections of histamine-in-beeswax.

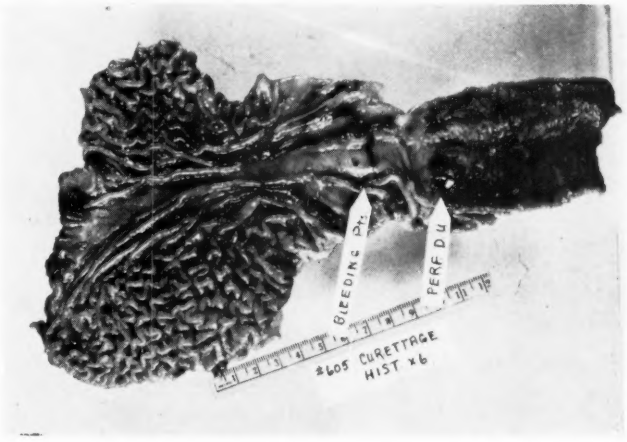

Fig. 5.—Perforated duodenal ulcer and antral bleeding points from Dog 605 (see Table II) subjected to curettage of the bone marrow of the right humerus in addition to six daily intramuscular injections of histamine-in-beeswax.

in a fasting state as soon after admission to the hospital as possible. Each analysis of gastric acidity (free and total) and volume was made on a one-hour specimen obtained by continuous aspiration and repeated on consecutive days. No drugs were administered during the period of aspiration.

Results of these studies are shown in Table III. There is no significant increase in the acidity or volume of fasting gastric secretions following fracture

of bones. Thus, there does not appear to be a stimulation of gastric secretion due to liberation of histamine at the fracture site as measured by gastric analyses. Ranges of gastric acidity and volume in the data recorded are in

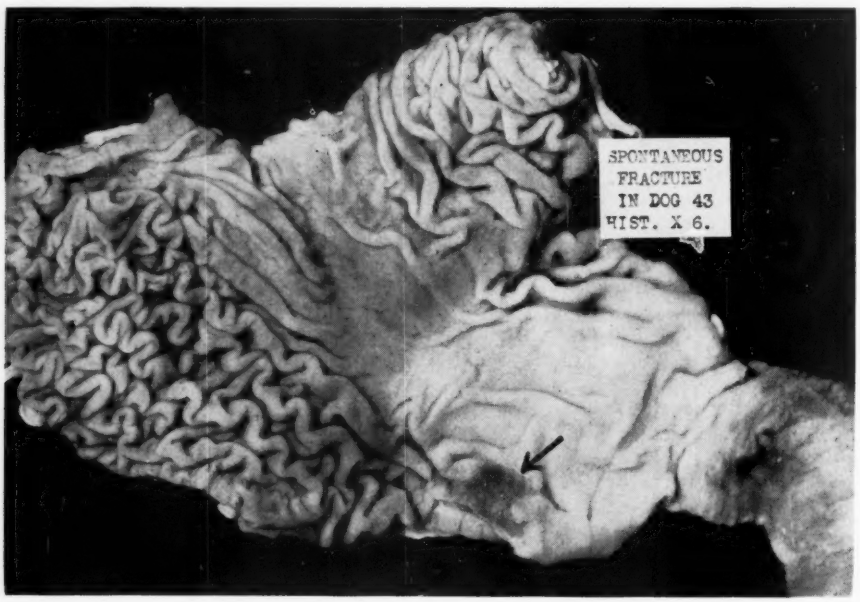

Fig. 6.—Gastric ulcer from Dog 43 with accidental fracture of both forelegs subjected to six daily intramuscular injections of histamine-in-beeswax. Arrow shows large antral ulcer.

Fig. 7.—Gastric ulcer from Rabbit 4 subjected to operative fracture and curettage of the bone marrow of the right humerus accompanied by six daily intramuscular injections of histamine-in-beeswax.

accord with normal values occurring in patients of similar age groups. It is to be noted that one patient (No. 9) in Table III is the same patient as one (No. 17) in Table I. Due to the occurrence of gastric hemorrhage after admission to the hospital, only one analysis of gastric acidity was determined.

TABLE III. STUDY OF THE GASTRIC SECRETORY RESPONSE IN CASES OF FRESH FRACTURE OF BONES IN MAN (NO HISTAMINE STIMULATION USED)

NO.	PATIENT	SEX	AGE (YR.)	FRACTURE	NO. OF ANALYSES	RANGE OF FREE ACIDITY°	RANGE OF TOTAL ACIDITY°	RANGE OF VOLUME C.C.
1	N. H.	M	69	Pelvis, sacrum, os calcis	6	0-0	12-68	3-13
2	E. C.	F	72	Left humerus	4	0-34	14-58	29-107
3	C. B.	F	75	Right femur	6	0-42	10-80	8-53
4	A. A.	M	60	Bilateral tibia and fibula with manipulation	3	8-40	24-52	103-204
5	A. K.	M	57	Left 10th to 11th ribs and 12th thoracic to 1st lumbar vertebrae	3	0-0	12-56	97-452
6	C. T.	M	68	Rt. femur with hip nailing	6	12-52	24-126	10-138
7	H. D.	M	46	Rt. ankle	5	0-26	14-44	12-133
8	C. McG.	F	65	Left femur (neck)	5	0-0	8-130	3-45
9	M. L.	M	17	Right femur	1	0	98	–
10	M. G.	F	63	Left femur	6	0-36	18-56	4-51

2. *Studies of Gastric Secretion Following Operative Fracture of Bones in Experimental Dogs Possessing Gastric Pouches.*—To further ascertain whether fracture of bones may produce an increase in gastric secretion, experiments were outlined employing dogs possessing isolated gastric pouches, on the thesis that a histamine-like stimulation effect would be reflected in the pouch secretions in dogs. Five Heidenhain (denervated) and two Pavlov (innervated) pouch dogs were used. Under intravenous sodium pentobarbital anesthesia six pouch dogs (five Heidenhain and one Pavlov) were subjected to drill holes with curettage of the bone marrow of the right humerus under sterile technique, the animals having been fasted eighteen hours prior to the experiments. All conditions were similar to those carried out in the preceding operations with dogs. Gastric pouch secretions were collected for a one- and two-hour fasting period, following which the animal was anesthetized and the operative procedure performed. Hourly samples of pouch secretions were collected, during the operation and for four subsequent hours. Studies of pouch secretions were made on these dogs every other day for four hours for twenty days. For control experiments one Heidenhain and one Pavlov pouch dog were subjected to nonspecific operations (appendectomy and splenectomy, respectively) and pouch secretions studied in the same manner as in the experimental dogs. On the day of operation on all dogs in this study control blood histamine values were determined as well as during and following the operation and in some cases for several subsequent days. Identical diets were maintained throughout the course of the experiments.

The results of this group of experiments are recorded in Table IV. It is noted that in only one dog (No. 145H) was there a marked stimulation of

TABLE IV. THE EFFECT OF VARIOUS OPERATIONS ON POUCH SECRETIONS IN DOGS

DOG NO.	OPERATION	EFFECT
Bone Operations		
145 (H)	Drill hole operation, rt. humerus	Marked stimulation* of acid and volume for 6 days post-operatively
129 (H)	Drill hole operation, rt. humerus	No stimulation effect
15 (H)	Drill hole operation, rt. humerus with destruction of the marrow by means of a pliable wire	No stimulation effect
20 (H)	Drill hole operation, rt. humerus with destruction of the marrow by means of a pliable wire	No stimulation effect
132 (H)	Operative fracture, rt. humerus	No stimulation effect
116 (P)	Operative fracture, rt. humerus	No stimulation effect
Nonspecific Operations		
20 (H)	Appendectomy	No stimulation effect
16 (P)	Splenectomy	No stimulation effect

*This effect of marked stimulation was not present when operation was repeated in four weeks.

gastric acidity and volume for six postoperative days. This was repeated in the same dog at a later time at which time no stimulating effect was noted. The blood histamine values showed no significant variation from normal levels.

3. *Studies of Gastric Secretion in Intact Dogs Subjected to Operative Fracture With Reference to Gastrointestinal Findings and the Occurrence of Fat Embolism.*—The following experiments were performed on a group of eighteen intact dogs having been placed on a standard diet of ½ pound horsemeat, 1 pound dog kibbles, per day, and water as desired. Experiments consisted of daily gastric intubations and aspiration of gastric juice for determinations of free HCl, total acidity, and reaction in terms of pH. After a period of standardization of six days, fifteen of the eighteen dogs were subjected to drill holes of the right humerous under intravenous sodium pentobarbital anesthesia employing sterile technique. Three control dogs were anesthetized only; no operative procedure was carried out. Daily gastric aspirations were carried out in all dogs until the completion of the experiments. The animals were sacrificed by an overdose of nembutal at regular intervals over a period of four weeks following the operative procedure. The three control dogs were sacrificed at six, twelve, and twenty-eight days after operation, respectively. All dogs were fed the standard diet each morning after gastric aspirations and food pans were removed each evening. Following operation no food was allowed until after the gastric aspiration of the following day. Water was allowed all dogs at all times. Upon sacrifice of each animal the gastrointestinal tract was examined and sections of the stomach, duodenum, brain, and lungs were obtained for microscopic study with reference to the occurrence of fat embolism.

Results of this study are recorded in part in Table V. It is noted that the determinations of free acidity before and after the drill hole operation of the humerus displayed no demonstrable differences in degree. Similarly, gastric

analyses of free acidity of the three control dogs were not significantly unlike the experimental dogs. Examination of the stomach and duodenum in the experimental dogs revealed the occurrence of erosion and/or ulcer or evidence of ulcer by healing scars in five of the fifteen dogs. The three control dogs displayed no abnormal findings upon sacrifice. It was noted also that the acute or active gastroduodenal lesions were present when the animal was sacrificed in three and four days, while lesions displaying chronicity occurred in ten, twenty, and twenty-two days, respectively. Mild gastritis and duodenitis were somewhat common findings. Microscopic findings are described later.

TABLE V. THE EFFECT OF EXPERIMENTAL FRACTURE UPON THE GASTRIC SECRETORY RESPONSE IN INTACT DOGS*

DATE	DOG NO.: 127	128	129	130	131	132	133	134	135	136	137	138	139	140	141	142	143	144
5/17	0°	0°	0°	15°	0°	24°	0°	0°	26°	0°	0°	0°	64°	20°	0°	0°	0°	0°
5/18	0	0	0	0	0	30	0	0	0	0	0	0	58	0	36.6	0	0	0
5/19	30	0	0	0	0	0	0	0	33.3	0	0	0	0	0	0	0	48	0
5/20	0	34	0	0	0	60	30	16	0	0	0	32	2.5	0	0	0	50	0
5/21	0	0	0	0	4	0	0	7.5	0	0	0	16	0	0	0	0	36	0
5/24	0	0	0	0	6	24	4	10	0	0	0	0	0	0	0	35	0	25
Operation																		
5/25	0	0	0	0	0	0	0	0	0	0	9	2.5	7.5	47	0	10	10	5.2
5/26		0	0	0	0	0	0	0	0	0	0	56	0	0	0	0	0	0
5/27			0	3.1	0	0	6	27.5	0	0	25	0	20	75	0	0	0	0
5/28				0	0	46	0	10	0	0	0	0	54	0	0	0	0	75
5/29					9	0	0	0	0	0	0	0	0	0	0	0	0	0
5/30						0	0	12	0	0	0	23.3	0	0	0	0	54.5	0
6/1							0	0	0	0	0	0	0	0	0	0	0	0
6/3								0	0	0	0	0	0	40	0	0	0	
6/5									48	14	0	28	46	0	46	0	64	
6/7										4	0	2	0	5	55	15.5		
6/9											0	0	50	0	60	0		
6/11												42	74	23.3	0	12.5		
6/13													0	0	6.6	66.6		
6/15														0	15	0		
6/17															0	0		
6/21															0	0		

*The body of the table represents measurements of free acidity of gastric juice obtained by daily gastric aspirations of fasting dogs, before and after a drill hole operation of the humerous. The dogs were sacrificed at varying lengths of time following operation. Three control dogs (No. 142, 143, and 144) were anesthetized only; no operative procedure was carried out. No significant differences in degree of gastric acidity were noted between operated and nonoperated dogs, nor in pre- and postoperative determinations.

It was concluded from these experiments that histamine liberation from the fracture site is not sufficient to cause stimulation of gastric acidity necessary to produce the gastric and duodenal lesions found in patients with fresh fracture or in the experimental dogs subjected to operative fracture.

D. ULCER PRODUCTION BY THE INTRAVENOUS INJECTION OF FAT INTO EXPERIMENTAL ANIMALS

On the thesis that the acute gastric and duodenal ulcers occurring in patients and animals sustaining or receiving fractures of long bones may be associated with the occurrence of embolism of fat, a study was outlined to determine whether ulcer could be produced experimentally by the intravenous injection of fat.

Observations were carried out in twenty-nine animals consisting of eleven rabbits, six cats, two guinea pigs, and ten dogs. Human breast or omental fat was employed, obtained from surgical procedures and extracted with ether. Fat, 1½ c.c. per kilogram of body weight, was injected intravenously. It has previously been stated that rabbits are quite refractory to ulcer production by histamine alone. In each of six rabbits, whose weights averaged 1.74 kilograms, a single intravenous injection of 1.5 to 2 c.c. of fat was made. Then 30 mg. of histamine-in-beeswax were implanted once daily for from one to four days.

Fig. 8.—Perforated ulcer in stomach of a rabbit after a single injection of 1.5 c.c. of human omental fat intravenously in addition to two daily intramuscular injections of histamine-in-beeswax.

No dietary strictures were imposed on the rabbits. A perforating ulcer occurred in each instance save one, and that rabbit died of pulmonary embolism shortly after the fat injection. Three rabbits were injected with fat but were given no histamine. Ulcer did not develop. In two additional rabbits, a daily implantation of 30 mg. of histamine-in-beeswax was made, in one over a period of twenty-one days, in the other for twenty-eight days; neither developed ulcer. Of six cats, each receiving a single intravenous injection of fat, two developed gastric ulcers, one at four, the other eighteen days after the fat injection. Of two guinea pigs injected with fat, both exhibited typical gastric ulcers. Of seven dogs given a single intravenous injection of fat, a bleeding duodenal ulcer was found in one dog sacrificed fourteen days after the fat injection. Of three dogs that received 30 mg. of histamine-in-beeswax daily following a single

intravenous injection of fat, all developed multiple bleeding duodenal and gastric ulcers within three days after the first injection of histamine.

In addition, four dogs, each possessing a gastric pouch, received a single intravenous injection of fat. Studies of gastric secretion in a fasting state before, during, and after injection of fat were carried out in each dog. It was found that intravenously injected fat does not stimulate nor augment gastric secretion.

Fig. 9.—Gastric ulcer from Cat 10 subjected to a single intravenous injection of nonemulsified human omental fat (1.5 c.c. per kilogram), sacrificed in four days.

E. THE ROLE OF FAT EMBOLISM IN THE OCCURRENCE OF GASTRODUODENAL ULCER AND/OR EROSION FOLLOWING FRACTURE IN PATIENTS AND EXPERIMENTAL ANIMALS, WITH REFERENCE TO THE FATE OF INTRAVENOUSLY INJECTED FAT

To determine the validity of the thesis that fat emboli are released from the site of fracture and lodge in the vessels of the gastrointestinal tract thus producing a local area of mucosal anemia susceptible to the acid-peptic digestive action of gastric secretions, sections of tissues involved were examined microscopically. Single blocks of tissue from the stomach, duodenum, brain, lungs, and kidneys were taken from several groups of animals in the previous experiments, as well as from a number of patients who died early after fresh fracture of long bones. Tissues were fixed in Zenker's solution, frozen, and stained with Sudan III. Emboli of fat thus are demonstrable as orange-colored globules within the blood vessels.

1. The occurrence of fat emboli attending the intravenous injection of fat in fifty-two animals is represented in Table VI. The influence of the time inter-

TABLE VI. INFLUENCE OF TIME INTERVAL ON OCCURRENCE OF FAT EMBOLI ATTENDING THE INTRAVENOUS INJECTION OF FAT IN LABORATORY ANIMALS (DOGS, CATS, RABBITS, AND GUINEA PIGS)

	NO. OF ANIMALS	AMT. OF FAT INJECTED (C.C. PER KG.)	PER CENT OF TISSUES REVEALING FAT EMBOLI			
			LUNG	BRAIN	KIDNEY	STOMACH
Sacrificed 1 to 4 days after fat injection						
A.	23	1½	91	60	73.9	47.8
Sacrificed 5 to 21 days after fat injection						
B.	29	1½	41	11.1	34.4	3.7

val, between the fat injection and the sacrifice of the animal, upon the incidence of demonstrable fat embolism in the various tissues is also shown. It is to be noted that the identification of fat in the stained sections was considerably higher, especially in the stomach, in the animals sacrificed and studied within one to four days after the fat was injected intravenously. In several instances, fat emboli within the submucosal vessels of the stomach were seen near or underneath the ulcers.

TABLE VII. OCCURRENCE OF FAT EMBOLI IN THE TISSUES OF DOGS SUBJECTED TO DRILL HOLE WITH CURETTAGE OF THE BONE MARROW OF THE HUMERUS, ACCOMPANIED BY HISTAMINE-IN-BEESWAX ADMINISTRATION

NO. OF DOGS	PER CENT OF TISSUES REVEALING FAT EMBOLI			
	LUNG	BRAIN	KIDNEY	STOMACH AND DUODENUM
Sacrificed 2 to 6 days after operative procedure				
19	68.4	36.8	47.4	26.3

Microscopic studies were carried out in nineteen animals (presented in Section B) which were subjected to drill hole and curettage of the bone marrow of the humerus accompanied by histamine administration. Single blocks of tissue from the stomach, duodenum, brain, lungs, and kidneys were examined. These animals were sacrificed from two to six days after operative fracture. The incidence of demonstrable fat embolism in the various tissues of these animals is shown in Table VII. In one instance fat globules were seen in the submucosal vessels immediately below an ulcer; in another instance, small fat particles were noted in mucosal capillaries under a superficial erosion of the stomach.

Microscopic studies were carried out on another group of experimental animals, eighteen dogs in which studies of gastric secretion following operative fracture had been carried out (Section C, 3). Single blocks of tissue from the

TABLE VIII. INCIDENCE OF THE OCCURRENCE OF FAT EMBOLISM IN PATIENTS WHO DIED EARLY AFTER FRACTURE OF LONG BONES

NO. OF PATIENTS	PER CENT OF TISSUES REVEALING FAT EMBOLI			
	LUNG	BRAIN	KIDNEY	STOMACH*
19	84.2	42.1	73.7	40.0

Average time interval between fracture and death, 7.9 days.

*Single blocks of the stomach were examined microscopically in fifteen cases; six showed definite evidence of fat embolism to the mucosal and submucosal vessels.

lung and the antrum and corpus of the stomach of these animals were examined. Three of these dogs had been controls, no operative procedure being carried out. Sacrifice of these animals ranged from one to twenty-eight days following the drill hole through the humerus. Fat emboli were demonstrable in the lung only in those dogs sacrificed six days or less after the operative procedure and, in one instance, fat embolism was noted in the vessels of a stomach in which there were numerous punctate hemorrhagic areas in the mucosa.

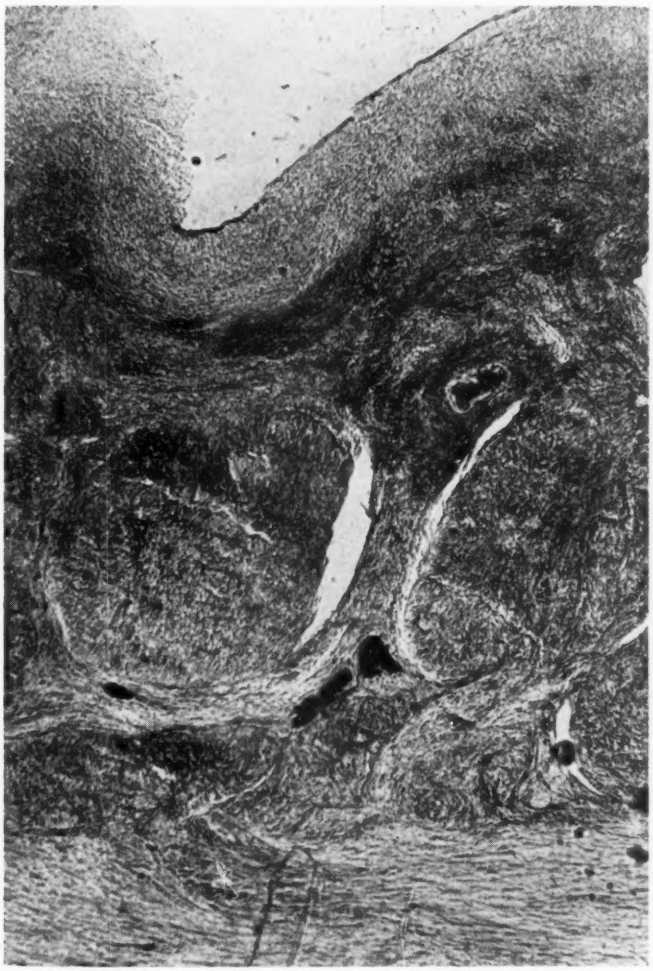

Fig. 10.—Photomicrograph illustrating embolic fat in submucosal vessels under the edge of an ulcer from the stomach of a dog subjected to curettage of the bone marrow of the right humerus and four daily intramuscular injections of histamine-in-beeswax. (Sudan III stain, magnification ×50.)

2. Studies relative to the incidence of fat embolism in patients were made on tissues of the stomach, brain, lungs, and kidneys, stained with Sudan III, obtained from the autopsy material of twenty-three patients, nineteen of whom died early after fresh fracture of the long bones. The incidence of the occurrence of fat embolism in the various tissues of these patients is shown in Table

VIII. The four control studies, carried out in patients who died of barbiturate poisoning, lobar pneumonia, epilepsy, and exposure to cold, exhibited no evidence of fat embolism microscopically.

It is noted that emboli of fat were demonstrable in the vessels of the lung in a greater incidence than observed in other organs studied. Single blocks of tissue from the stomach of fifteen of the patients who died early after fracture revealed an incidence of 40.0 per cent of emboli of fat within the submucosal or mucosal vessels in the stomach. Petechial mucosal bleeding was seen microscopically adjacent to a mucosal vessel of the stomach occluded by a fat embolus.

Fig. 11.—Photomicrograph illustrating embolic fat in the vessels at the base of a duodenal ulcer from patient A. H. (see Table I, Case 23), who died twelve days after fracture of the right femur. Massive hematemesis persisted after it had occurred on the ninth hospital day. At autopsy there was evidence of generalized fat embolism.

DISCUSSION AND INTERPRETATION OF RESULTS

Observation of hematemesis from gastroduodenal ulcer and/or erosion complicating fracture of long bones prompted a study of case records of patients who died early of fracture (reports collected from the files of the Department of Pathology of the University of Minnesota). The incidence of acute gastroduodenal ulceration in cases of fresh fracture of long bones coming to autopsy over a twenty-four-year period was 27 in 1,432, or 1.88 per cent. In well over one-half of the cases collected, no clinical or pathologic diagnosis of fat embolism per se was noted or apparently looked for; however, the course of the illness of each case, in retrospect, is highly suggestive—a majority developing dyspnea, mental confusion, or oliguria, some exhibiting petechiae of the skin, hematemesis, or melena. Clinical diagnoses of acute ulcer with institution or specific therapy were made in seven (24.1 per cent) instances, five coming to

autopsy, at which time the diagnosis was substantiated. The incidence of hemorrhage from the gastrointestinal tract in the cases presented was 58.6 per cent, being recognized clinically in 41.4 per cent.

It should be mentioned that a great number of fracture patients submitted to necropsy died almost immediately following the injury—too short a time for the occurrence of gastroduodenal ulceration from fat emboli. Similarly, ulcers may be healed over in cases coming to necropsy late after fracture.

It is apparent, when an attempt was made to place the observations made clinically upon an experimental basis, that ulcers can be produced by experimental fracture and drill hole with curettage of the bone marrow in the dog, an animal in which the spontaneous occurrence of ulcer is not known. Moreover, when gastric secretion is stimulated maximally by the administration of histamine implanted in beeswax, the rate of occurrence is increased; conversely, subjection of the animals to operative fracture hastens the development of the histamine-in-beeswax provoked ulcer in the dog. Similarly, when rabbits are subjected to fracture in addition to histamine administration, gastroduodenal ulcers may be produced, a result which is not obtainable in rabbits receiving histamine-in-beeswax alone. Thus it may be said that experimental fracture or curettage of the bone marrow abets the ulcer diathesis.

One of the thirteen rabbits subjected to fracture accompanied by histamine-in-beeswax administration developed a gastric ulcer. A higher incidence may have been expected except, as Scriba[5] pointed out, that the femur of a 2 kilogram rabbit contains an average of only 1.3 Gm. of fat.

In the studies in which experiments were designed to determine the mechanism of the production of gastroduodenal ulcer and/or erosion following experimental fractures in animals, it is found that stimulation of gastric secretion due to histamine liberation from the site of trauma is not a significant factor. Gastric secretory values of free and total acidity and volume, as well as blood histamine levels, in both intact and pouch dogs subjected to operative fracture indicate little, if any, departure from normal values.

The reproduction of the phenomenon of fat embolism occurring in fractures by the employment of intravenous injection of fat in animals, with and without administration of histamine, reveals similar findings as those present in animals subjected to actual fracture or curettage of bone marrow. The intravenous injection of fat does not augment gastric secretion as studied in pouch dogs.

Finally, the demonstration of fat emboli within the submucosal and mucosal vessels of the stomach and duodenum, in addition to other organs, of the animals receiving experimental fracture, as well as in the organs of a number of patients dying early after fracture and amputation, leaves little doubt that the occurrence of gastroduodenal ulcer and/or erosions following fracture of long bones is a concomitant of fat released from the site of fracture. The mechanism of ulcer production following fracture then is, undoubtedly, that of plugging the end vessels to the mucosa; the resultant anemic areas in the mucosa become less resistant to injury and digestion by the acid-peptic juice of the stomach, than is the normal mucosa.

It is interesting to note, in animals studied at various intervals after the intravenous injection of fat, that the rate of disappearance of the fat from the mucosal and submucosal vessels is rapid. This circumstance undoubtedly accounts for the fact that hematemesis, erosions, or ulcers have not been observed more commonly to accompany fracture of long bones in man.

SUMMARY

1. A study of the incidence of gastroduodenal ulcer and/or erosion complicating fracture and amputation of long bones in man was made. A tabulation of twenty-seven cases of acute gastroduodenal ulcer or erosion in patients dying of fracture of long bones among 1,432 cases of fracture over a period of 26½ years, together with two such cases with recovery, is presented. Two similar cases following amputation are also presented.

2. A study was made concerning the experimental production of gastroduodenal ulceration and/or erosion in laboratory animals by fracture of curettement of the bone marrow, with reference to the ulcer diathesis.

3. Studies were carried out concerning gastric secretion in clinical cases of fresh fractures of long bones and after operative fracture in experimental animals, together with studies of the histamine levels of the blood after experimental fractures in animals.

4. Experiments regarding ulcer production by the intravenous injection of fat into experimental animals were carried out, constituting a reproduction of the phenomenon of fat embolism in experimental animals.

5. Microscopic studies were carried out to evaluate the role of fat embolism in the occurrence of gastroduodenal ulcer and/or erosion following fracture in patients and experimental animals, with reference to the fate of intravenously injected fat.

CONCLUSIONS

1. Gastroduodenal ulcer and/or erosions, with resultant hemorrhage, are an occasional complication of fracture and amputation of long bones in man.

2. Gastroduodenal ulcers and/or erosions can be produced in experimental animals by operative fracture or curettage of the bone marrow; the incidence of such erosions or ulcers is markedly increased when histamine administration accompanies the fracture, especially in dogs. Experimental fracture of long bones abets the ulcer diathesis.

3. Gastroduodenal ulcers and/or erosions can be produced by the intravenous injection of small amounts of fat; this reproduction of the phenomenon of fat embolism also increases the susceptibility of the laboratory animal to the histamine-provoked ulcer.

4. Emboli of fat can be demonstrated in the submucosal and mucosal vessels of the stomach and duodenum, not only in experimental animals subjected to operative fracture, but also in patients dying early after fracture of long bones. The rate of disappearance of the fat from the tissues is rapid.

5. The mechanism of the occurrence of gastroduodenal ulcer and/or erosions following fractures or amputations of long bones is undoubtedly one of

embolic occlusion of the vessels to the mucosa by fat released from the fracture site; the resultant anemic areas in the mucosa become susceptible to the acid-peptic digestive activity of the gastric juice.

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Editorial

A New Policy

BEGINNING with this issue, SURGERY will each month contain a signed editorial dealing with some aspect of medicine, surgery, or experimental science. Some of these will deal with the work of the author; some will be of the general informative type, while others will without doubt be provocative. In order that the objectives be reached, the editorial policy will be as catholic as possible. There is a dearth of good writing in many of the papers now being published in our journals. There is a shocking lack of propriety by many authors in failing to give proper credit for well-deserved priority. There is all too frequently an unnecessary verbosity in our papers, so that not only are paper and print wasted, but the reader's time is unnecessarily wasted. Too frequently conclusions are not based upon the data presented, and all too frequently significance is attached to data that are not significant. The statements made in a paper are often accepted as true merely because one or more of the authors is well known. A preliminary report to gain priority is often not published as a preliminary report, and yet time and again no subsequent report is published because additional studies fail to verify the original statements. The responsibilities of authors to their reading audience are great, but not always fulfilled. These are matters of real concern to many of the people interested in the best aspects of medicine in its broadest sense. The editorials to be published will not be agreed with by all our readers. To hope that they will be would be foolish, nor does SURGERY accept any responsibility for what each author says. We shall engage in no polemics, but we shall be happy to hear from those of our readers who believe that the subjects are not fairly presented.

—I. S. RAVDIN

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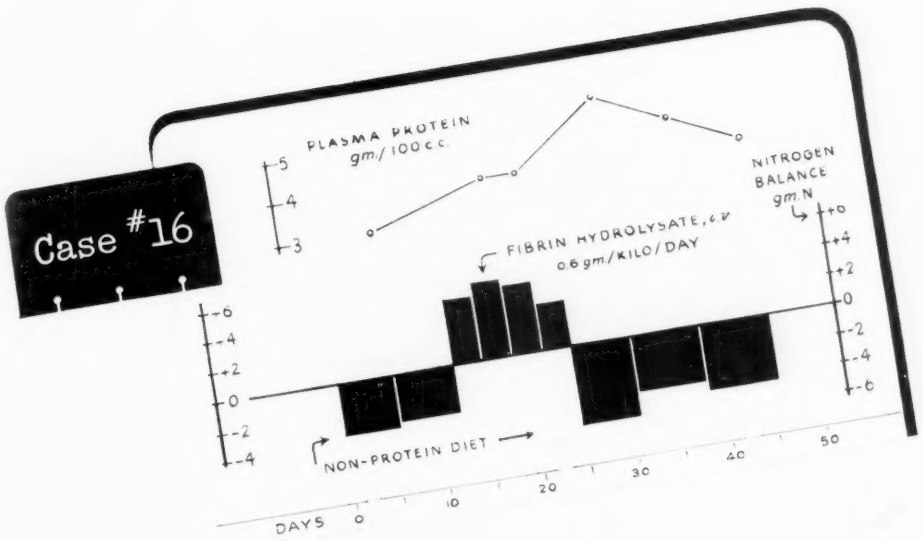

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